The New England
Journal of Medicine

Copyright, 1942, by the Massachusetts Medical Society

VOLUME 226 APRIL 2, 1942 NUMBER 14

OPTIMAL DOSAGE AND THE RECIPROCAL RELATION OF DESOXYCORTICOSTERONE ACETATE AND SODIUM IN ADDISON'S DISEASE*

THOMAS H. MCGAVACK, M.D.†

NEW YORK CITY

DESOXYCORTICOSTERONE is a readily available ketosteroid of the adrenal cortex and has greater life-maintaining qualities than any chemically pure constituent isolated to date.[1-5] Nevertheless, such extreme practical difficulties have been encountered in its clinical application in cases of Addison's disease[6-9] as to lead to its condemnation in certain quarters.[6, 9]

The drug affords satisfactory replacement therapy for adrenocortical deficiency so far as the vital and sodium-regulating factors are concerned. Moreover, it enables the animal to store and use carbohydrate food and exogenous protein satisfactorily, but fails to restore the ability of the organism to produce sugar and glycogen from endogenous protein and fat. If properly used, it enables the patient with Addison's disease to resume his usual daily activities.

The dangers in the application of desoxycorticosterone have been centered around its predominant effect on electrolyte metabolism — with particular reference to sodium. The early failure to understand clearly the extent of this action has been responsible for the untoward reactions observed. Wholesale condemnation of the drug on this basis alone seems presumptuous, since very few useful additions to the therapeutic armamentarium of the physician have been without limitations.

It has been shown that sodium and desoxycorticosterone exert a similar beneficial action in the adrenalectomized animal, and that although salt in sufficient quantity in such animals maintains life, it does not afford the same vitality as a combination of the two agents.[10, 11] The ability of desoxycorticosterone to prevent salt loss and to correct faulty potassium exchange in the subject with adrenal insufficiency is its best known action. At the same time, it is the one that has led to most of the complications.

During the last two and a half years, 6 cases of Addison's disease have been treated with desoxycorticosterone acetate, together with regulation of the sodium and potassium intake. From observation on this group of patients, two conclusions concerning the efficacy and safety of desoxycorticosterone as a therapeutic agent can be drawn: the patient with Addison's disease can be satisfactorily maintained in good health by the judicious use of desoxycorticosterone acetate and the simultaneous regulation of sodium and potassium intake; and within certain limits, a reciprocal relation exists between the amount of sodium to be ingested and the dose of desoxycorticosterone acetate necessary to maintain the subject in good condition.

The criteria of "maintenance in good condition" include a sense of well-being on the part of the patient, a slow, steady gain in weight or a maintenance of normal weight once attained, a return of blood pressure to normal and its fixation there, a gradually rising cardiothoracic ratio, — not to be allowed to exceed 0.50, and preferably maintained around 0.46, — normal values for sodium and potassium in the blood serum and urine, and improvement toward normal in the configuration of glucose-tolerance curves.

The repeated determination of the blood sodium and potassium values and of the glucose-tolerance curve is comparatively difficult for the average practitioner and often barred by the expense entailed to the patient. Such determinations are not essential, so long as the other reasonably simple procedures are carried out. Rapidly rising cardiothoracic ratios should be avoided. This point warrants some emphasis. In no case have I seen hypertension or edema whose onset was not preceded by rather sudden changes upward in the

*From the Department of Medicine, New York Medical College, and the Medical Service, Flower and Fifth Avenue Hospitals and Metropolitan Hospital.

†Associate professor of medicine, New York Medical College; visiting physician, Flower and Fifth Avenue Hospitals; visiting physician, Metropolitan Hospital.

ratio between the transverse diameter of the heart and the transverse diameter of the chest. Since these patients almost invariably need a roentgenogram of the heart and lungs as a part of the initial diagnostic survey, subsequent changes can be compared to the size of the heart as obtained in this first study. If necessary, these changes may be charted in the office even less expensively by orthodiascopy.

Signs of overdosage with desoxycorticosterone acetate include a sudden gain in weight, hypertension, a cardiothoracic ratio above 0.50, edema of any part of the body (late manifestation) and a definite feeling of malaise not unlike that prior to the administration of any treatment for the disease. Indeed, in the early handling of patients by the use of desoxycorticosterone acetate, these symptoms were considered an aggravation of the state of adrenal insufficiency, and more of the drug was administered.[9] Manifestations may vary from patient to patient, but the extreme sense of fatigue and weakness that is so characteristic of the Addisonian state itself is common to all patients. On three occasions, I have observed signs of overdosage, in no case resulting seriously.

Using the criteria mentioned, it has been possible to bring about in these 6 patients with Addison's disease a state of stabilization sufficiently good to permit each to return to his previous walk in life. Particular care has been taken to regulate sodium intake and desoxycorticosterone dosage reciprocally, since failure to recognize the dangers of too much of one in relation to the other appears to have caused the difficulties seen in the management of the disease. To analyze the results, each change of sodium administered or desoxycorticosterone used has been charted in relation to the other, and the state of health of the patient carefully checked while on each such variation of his regime (Fig. 1).

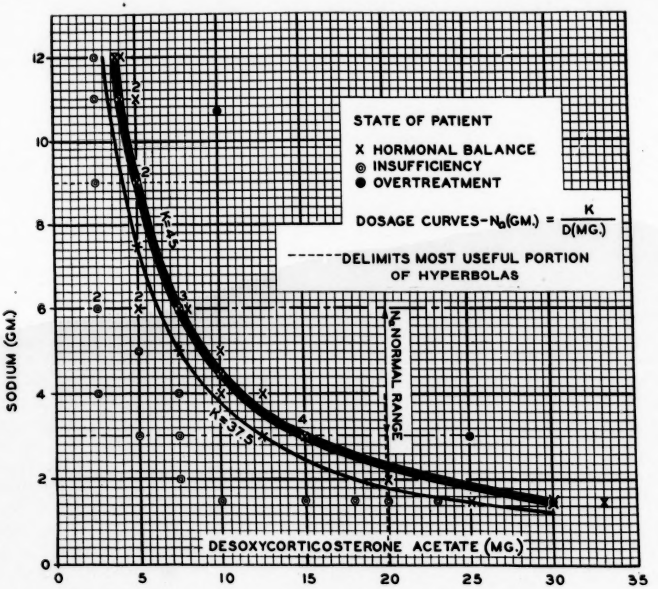

FIGURE 1. *Clinical Results in 6 Cases of Addison's Disease following the Use of Forty-seven Different Ratios for the Daily Intake of Sodium and Desoxycorticosterone Acetate.*

The numerals indicate the number of cases represented by a given point.

The amount of sodium and desoxycorticosterone acetate given daily was recorded for each of the 47 trial periods. The patient remained on each of the changes made for not less than six weeks, except in those cases in which signs of overdosage became apparent, or in those in which signs of insufficiency were severe before such a period was completed. As judged by the criteria already mentioned, the

patients were in hormonal balance in 28 of the trial periods, in insufficiency in 16, and subject to complications in 3. If an attempt is made to pass a curve through a majority of the plotted points in which a balanced ratio between sodium and desoxycorticosterone exists, the pattern of such a curve clearly becomes that of a hyperbola, $Na = k \div D$, where Na represents the daily intake of sodium in grams, D the daily dose of desoxycorticosterone acetate in milligrams, and k the constant. When substitutions were made in this formula from figures used in ascertaining the optimum dosage in a number of cases, k equaled 45 in 14 periods and 37.5 in 4, and in the remaining 10 periods, lay between 30 and 37.5 in 2, between 37.5 and 45 in 2, and between 45 and 55 in 6. In other words, a hyperbola with the formula, Na (gm.) $= 45 \div D$ (mg.), passes through 14 of 28, or 50 per cent, of all the trials during which the patient was shown to be in a satisfactory state of balance; the next greatest frequency is given by the formula, Na (gm.) $= 37.5 \div D$ (mg.), which passes through 4 of 28, or 14 per cent, of the points of optimal dosage plotted. No complications arose when ratios lay close to those indicated by either of these curves or by points between them. The area between them might be spoken of as the "zone of safety" for the selected dosage of sodium and desoxycorticosterone acetate. My experience suggests that dosages should lie closer to the first-mentioned curve with a constant of 45 (heavier line). It seems obvious, however, that no predetermined ratio for sodium and potassium is satisfactory in all cases, since the degree of adrenal insufficiency varies from patient to patient. Nevertheless, from present evidence, this variation takes place over a rather narrow range of equivalents, in contrast, for example, to the wide variation of insulin dosage necessary in the treatment of patients with diabetes mellitus. Such a difference can possibly be explained on the basis that thus far it has been impossible to produce "grades" of adrenal insufficiency experimentally. The operator either removes so much of the gland that the animal dies, or by leaving even the slightest fraction more, enables the animal to survive, apparently in the best of health.

As with any other biologic relation capable of expression in a hyperbolic curve, limits of applicability are in evidence. My observations suggest that patients do best when the daily intake of sodium is varied between 2.3 and 9.0 gm., and that of desoxycorticosterone acetate from 5 to 20 mg. (Fig. 1). Patients on a higher quantum of sodium with concomitantly less desoxycorticosterone had less endurance and, in general, felt "less fit" than when the ratios noted above were observed. Moreover, higher dosages of desoxycorticosterone were associated with more nearly normal glucose-tolerance curves,[12] although carbohydrate metabolism could not be regarded as completely normal in any case. The highest doses of desoxycorticosterone acetate — 20 to 33 mg. — have been quite satisfactory from the patients' point of view. The majority state that they "feel fine." Despite the concomitantly low salt intake, however, blood pressures tend to remain at upper normal levels, and it has been suggested that some storage of sodium, with possible "packing" of the cells, may be taking place.[13, 14] It seems logical and practical to make the range of dosage of desoxycorticosterone conform to the normal range of sodium intake (3 to 6 gm.) as indicated by the interrupted line in Figure 1. If this is done, it appears that from 7.5 to 15.0 mg. of desoxycorticosterone acetate can be given daily over relatively long periods. I had originally gained the impression that such a dose was too high for continued use without careful supervision of the patient; this may yet be proved true, for it is quite possible for some regeneration of cortical tissue to take place, or for aberrant tissue to initiate functional activity. If the curve of the lower constant (37.5) is used, this dosage in the range mentioned lies between 6.3 and 12.5 mg. daily. I consider this a perfectly safe amount in any patient with proved Addison's disease.

Previously stabilized patients in whom the product of sodium in grams and desoxycorticosterone in milligrams was changed to 15 or less (6 trials) quickly developed obvious signs of adrenal insufficiency, with a loss of weight, a fall in blood pressure, cardiothoracic ratio and blood serum sodium, and a return of progressive weakness. Such low values should be completely avoided when one plans the therapeutic regime of the patient with Addison's disease.

Three patients showed signs of toxicity from overtreatment. Two of these are as follows:

Case 1. H. L. had been receiving 10.7 gm. of sodium and 10 mg. of desoxycorticosterone acetate daily for 9 days, when she developed swelling of the ankles, puffiness about the eyes, slight dyspnea and increased weakness. There was no pulmonary edema, but the heart was markedly enlarged, with a cardiothoracic ratio of 0.58, a heart volume of 693.0 cc. per square meter of body surface, and a blood volume of 5963 cc. (theoretic normal, 4466 cc.). Sixteen days previously, these values had been 0.41, 328.8 cc. and 3507 cc., respectively. This patient was later given 15 mg. of desoxycorticosterone acetate daily when the sodium intake was limited to 3 gm. For 6 months, there were no untoward effects. It is obvious, therefore, that the toxic reaction was not a factor of the drug alone, but was produced by the interaction of the steroid with available sodium.

Case 2. J. F., a 60-year-old man, was in an extremely emaciated condition, bordering on crisis, when first coming under treatment. For 6 months, he had suffered from a continuous diarrhea, with severe, intermittent,

FIGURE 2. *Serial Variations in Teleroentgenographic Shadows in Case 2 while the Patient was on a Constant Intake of Sodium and a Changing Dosage of Desoxycorticosterone Acetate.*

crampy, upper abdominal pain. Throughout treatment, he was maintained on a daily dosage of 3 gm. of sodium. It was necessary to give him 25 mg. of desoxycorticosterone acetate daily before the abdominal symptoms were completely controlled, although he had shown improvement in his general condition when the amount of steroid was 15 mg. He showed no signs of toxicity from 25 mg. daily until the end of 2½ weeks, when the blood pressure was 148/84 (normal for 60 years of age) and other factors, such as a sense of well-being, weight and serum electrolytes, were within normal limits, but the cardiothoracic ratio had increased from 0.45 to 0.51 (Fig. 2 and Table 1).

One week after changing to 1.5 gm. of sodium and 30 mg. of desoxycorticosterone acetate daily, the patient developed mild occipital headaches and slight ankle edema. The weight, blood pressure and cardiothoracic ratio, which had previously been 58.6 kg., 140/72 and 0.42, respectively, became 59.0 kg., 164/120 and 0.48, respectively. Subjectively, the only symptom was headache, which never required medication. Within a week, the edema subsided, the headaches disappeared, and the blood pressure returned to within normal limits (138/85). The patient was maintained on the same regime for an additional 3 weeks, and continued to gain in weight and strength. The cardiothoracic ratio was stabilized at 0.46, the serum sodium remained within normal limits, and, moreover, the absorption and utilization of glucose, as indicated by the oral glucose-tolerance curves, improved materially.

TABLE 1. *Changes in Cardiothoracic Ratio in Case 2.*

X-RAY FILM (FIG. 2)	DATE	CARDIOTHORACIC RATIO	BLOOD PRESSURE	DESOXYCORTICOSTERONE ACETATE	COMMENT
			mm. Hg.	*mg.*	
A	1/23/41	0.38	70/50	0	Cortical insufficiency
B	3/12/41	0.45	95/65	5 (1 week) 10 (2 weeks)	
C	4/5/41	0.45	100/70	20 (2 weeks)	Good clinical condition
D	4/23/41	0.51	116/72	25 (2½ weeks)	"Feels fine," and gaining rapidly; note high cardiothoracic ratio; sodium desoxycorticosterone product high at 75.
E	4/30/41	0.53	148/84	25 (1 week)	Went into cardiac failure on this date; note the normal blood pressure but high cardiothoracic ratio.
F	5/22/41	0.50	132/80	15 (3 weeks)	Lung fields clearing; cardiothoracic ratio decreasing; sodium desoxycorticosterone product normal at 45.

In spite of the rise of the ratio above 0.50, it was decided to continue the previous regime, to complete special studies reported elsewhere.[12] One week later, the blood pressure had risen to 148/84, the cardiothoracic ratio to 0.53, and the patient suddenly developed ankle and pulmonary edema, breathlessness, dilatation of the heart and weakness.

The second case demonstrates the fact that the cardiothoracic ratio is one of the earliest and most sensitive indicators of overdosage. I still believe that ratios should be maintained in the neighborhood of 0.46,[15] to avoid any possible danger of toxic manifestations, although outspoken symptoms have not been seen with any ratios below 0.51. This is the only case in which frank cardiac failure occurred. Such a disturbance appeared only after three and a half weeks on a drug and sodium ratio nearly twice that which would have been indicated by the "dosage curves" of Figure 1. This certainly suggests that the drug can be used without danger in the average case, if proper attention is paid to simple rules of administration.

The third reaction observed, which was a most interesting and yet a very mild one, disappeared without any change in treatment.

CASE 3. E. M., a 24-year-old man, for over a year was comfortably stabilized on a daily sodium intake of 6 gm. and a sufficient number of pellets by implantation to yield 2.5 mg. of hormone daily.*

*By trial-and-error removals and weighings in this and 3 other cases, it was estimated that each 150-mg. pellet of desoxycorticosterone acetate from the source available (Schering Corporation) gives a daily absorption of 1 mg. Each milligram so absorbed appears to equal 3 mg. of material when injected in oily suspension. It is essential to know the source of pellets for implantation, since the shapes, sizes and hardness alter the rate of absorption and vary considerably with different manufacturers.

This is the only case in which a reaction occurred when the product of the daily ration of sodium in grams and desoxycorticosterone acetate in milligrams was 45 or less. The fact that the reaction disappeared spontaneously is not explained. It has been suggested that with such high doses of hormone — despite the concomitantly very low ingestion of salt — a packing of sodium into the interstitial spaces and into the cells themselves must occur.[13, 14] It therefore seems unwise in the present state of knowledge to utilize the proportions suggested by the extreme right end of the hyperbolic curve for very long periods.

SUMMARY

Forty-seven variations in the ratios of sodium and desoxycorticosterone acetate used in the management of 6 patients with Addison's disease were plotted with respect to each other.

In 28 trial periods, the patient was in hormonal balance, that is, in good clinical condition with normal values for weight, blood pressure, cardiothoracic ratio and serum electrolytes. In 3, there were signs of toxicity from overdosage, and in the remaining 17 there was clinical and laboratory evidence of adrenal insufficiency.

All the ratios representing patients in "good clinical condition" have been shown to lie on, near or between the portions of two hyperbolic curves, whose constants are 37.5 and 45 respec-

tively. Fourteen actually lay on the latter curve. The area between these curves may be spoken of as the "zone of safe dosage."

As a general rule, patients felt best and showed most nearly normal carbohydrate utilization on dosages of hormone ranging between 10 and 20 mg. daily, with corresponding values for sodium, whereas larger doses did not augment these effects materially. Patients receiving less than 5 mg. of hormone daily, and concomitantly more than 9 mg. of sodium daily, did not "feel fit," despite the maintenance of weight, blood pressure and serum electrolytes within a normal range of values.

Conclusion

Patients with Addison's disease can be safely and satisfactorily treated with desoxycorticosterone acetate, provided that attention is paid not only to the usual criteria of well-being, but also to the regulation of the dosage of drug and intake of sodium in a reciprocal manner. Values for these two variables represented by points lying on or between portions of hyperbolic curves in which the constants are 37.5 and 45, respectively, have been found to yield satisfactory results in clinical cases of insufficiency of the adrenal cortex.

1 East 105th Street

References

1. Wells, B. B., and Kendall, E. C. The influence of the adrenal cortex in phlorhizin diabetes. *Proc. Staff Meet., Mayo Clin.* **15**:565-573, 1940.
2. Ingle, D. J. The effect of two cortin-like compounds upon the body weight and work performance of adrenalectomized rats. *Endocrinology* **27**:297-304, 1940.
3. Gordon, E. S. The use of desoxycorticosterone and its esters in the treatment of Addison's disease. *J. A. M. A.* **114**:2549-2551, 1940.
4. Sevringhaus, E. L. Desoxycorticosterone acetate in Addison's disease. Reese, Lewis and Sevringhaus's *Yearbook of Neurology, Psychiatry and Endocrinology*. 856 pp. Chicago: Year Book Publishers, 1940. P. 703.
5. Ingle, D. J., and Thorn, G. W. A comparison of the effects of 11-desoxycorticosterone acetate and 17-hydroxy-11-dehydrocorticosterone in partially depancreatized rats. *Am. J. Physiol.* **132**:670-678, 1941.
6. Ferrebee, J. W., Ragan, C., Atchley, D. W., and Loeb, R. F. Desoxycorticosterone esters: certain effects in the treatment of Addison's disease. *J. A. M. A.* **113**:1725-1731, 1939.
7. Wilder, R. M. Progress in treatment of Addison's disease. *Proc. Staff Meet., Mayo Clin.* **15**:273-277, 1940.
8. Kuhlmann, D., Ragan, C., Ferrebee, J. W., Atchley, D. W., and Loeb, R. F. Toxic effects of desoxycorticosterone esters in dogs. *Science* **90**:496, 1939.
9. McCullagh, E. P., and Ryan, E. J. Use of desoxycorticosterone acetate in Addison's disease. *J. A. M. A.* **114**:687, 1940.
10. Anderson, E., Herring, V., and Joseph, M. Salt after adrenalectomy: carbohydrate stores in adrenalectomized rats given various levels of sodium chloride. *Proc. Soc. Exper. Biol. & Med.* **45**:488-493, 1940.
11. Anderson, E., and Herring, V. Effect of NaCl and desoxycorticosterone on body weight and carbohydrate stores of adrenalectomized rats. *Proc. Soc. Exper. Biol. & Med.* **43**:363-366, 1940.
12. McGavack, T. H., Charlton, G. P., and Klotz, S. The effect of desoxycorticosterone acetate on glucose tolerance in normal individuals and in patients with Addison's disease. *J. Clin. Endocrinol.* **1**:824-830, 1941.
13. Miller, H. C., and Darrow, D. C. Relation of serum and muscle electrolyte, particularly potassium, to voluntary exercise. *Am. J. Physiol.* **132**:801-809, 1941.
14. Thorn, G. W. Personal communication.
15. McGavack, T. H. Changes in heart volume in Addison's disease and their significance. *Am. Heart J.* **21**:1-16, 1941.

AN IMPORTANT ETIOLOGIC FACTOR IN SO-CALLED "FOOT STRAIN"*

Robert B. Osgood, M.D.†

BOSTON

Robert Louis Stevenson once said that after the old man has listened to the young man, the old man usually remarks, "Well, my boy, I thought that at your age." We older men will do well if we constantly remember Stevenson's comment to the effect that the old man's remark suggests that "the young man was probably right." Nevertheless, if as we grow older we can manage to keep a reasonably open mind and do not ride our hobbyhorses too hard, experience may be the worthy teacher that it is proverbially said to be. Consequently, I have the temerity to call attention to what I believe to be an important and somewhat neglected etiologic factor in foot strain or, as the condition is still erroneously called, "flat foot." The subject is hackneyed, but the sufferers from foot strain are still many.

May I refresh your minds as to the essential rudimentary anatomy of bipedal symptomless weight bearing?

Good posture, which conforms to the lines of gravity, will be taken for granted. The normal lines of weight bearing, transmitted as they are

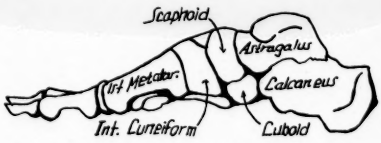

Figure 1. *Medial Aspect of the Bones of the Foot.*

through the tibias, fall considerably to the inner or medial sides of the feet. So far as the bony anatomy of the lower leg and foot is concerned,

*Read at the annual meeting of the New England Surgical Society, Hanover, New Hampshire, September 6, 1941.

†John Ball and Buckminster Brown Professor of Orthopaedic Surgery Emeritus, Harvard Medical School.

the lines of weight bearing tend to depress the feet on their medial aspects. What resists this straining force? Neither of the two bony arches of the foot—the longitudinal arch from the os

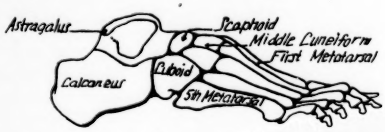

FIGURE 2. *Lateral Aspect of the Bones of the Foot.*

calcis to the metatarsal heads and the anterior transverse arch formed by the heads of the metatarsal bones—has any keystone worthy of the name (Figs. 1 and 2). One, therefore, cannot depend on the bony configuration to resist this deforming, inward, sagging force. The weight is transmitted through the tibia to the astragalus at the ankle joint, and thence to the os calcis and the ground. The main joint between the astragalus and the os calcis is a shallow ball-and-socket joint, but the projection of the sustentaculum tali on the inner side of the os calcis offers a prop that would keep the astragalus from rolling medially or inwardly, provided the os calcis could retain the vertical plane. The os calcis is held in this vertical plane by the strong posterior calcaneoscaphoid and the tibioastragaloid or deltoid ligaments, the plantar ligaments and the capsules of the joints of the tarsal bones (Fig. 3). These

FIGURE 3. *Ligaments Supporting the Os Calcis.*

ligamentous structures are only passive supports and will stretch and weaken if a continuous force such as faulty weight bearing is active.

By far the major factors that maintain proper weight-bearing lines in the feet are the muscles of the lower leg, which have their insertions in the feet, and to a lesser extent, the intrinsic muscles of the feet themselves. These are active, not passive, supports.

Duchenne[1] (1806–1875), that brilliant son of a Boulogne sea captain, invented an electric apparatus that determined the exact function and comparative strength of the muscles by stimulating their contraction. It had previously been necessary to make skin incisions and to stimulate the muscles by actual contact. His invention of moist electrodes over the muscle bellies did away with

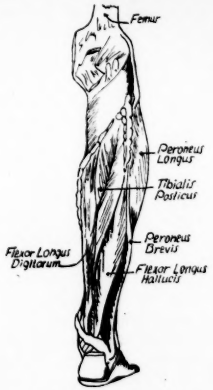

FIGURE 4. *Posterior View of the Muscles of the Lower Leg.*

the necessity for surgery and enormously simplified the study of muscle function. One of the many increments of knowledge that this careful pioneer added came from his study of the muscles of the lower extremities in relation to weight bearing. He reached the conclusion that faulty weight bearing and foot strain were most commonly caused by a faulty balance between the group of muscles that inverted the foot and elevated the arches and the group whose contraction tended to evert the foot and depress the arches. His conclusion was sound, but few seem to have applied it to the relief of foot strain.

Figures 4 and 5 illustrate the principal muscles of these two synergistic but more or less antagonistic groups. The first group may be called the inverters or the maintainers of symptomless weight bearing; if the second—the everters—overbalances the inverters, foot strain usually results.

Many years ago, I was interested in several patients who consulted me because they had been rejected for the fire and police departments because of "flat feet." They protested that they had never

had any symptoms from their pedal extremities, and a few of them boasted of their prowess as long-distance walkers and of the prizes they had won in track sports. When they stood, their feet were certainly flat, but when they walked or ran their weight-bearing lines were perfect. Apparently, the fire and police departments had rejected excellent men because when they stood their feet were flat. I determined, therefore, in 1907, to make a study of the comparative strength in pounds pull of the two antagonistic groups of the inverters or adductors and the everters or abductors. A simple and fairly foolproof apparatus was devised, which is illustrated by Figure 6.

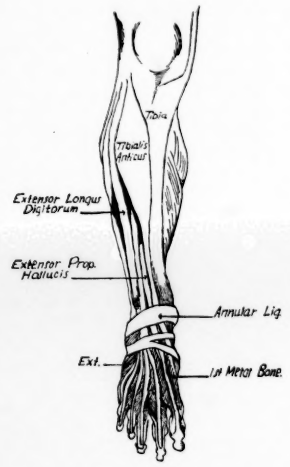

FIGURE 5. *Anterior View of the Muscles of the Lower Leg.*

The late Dr. Arthur T. Legg was then in charge of the large foot clinic at the Carney Hospital, and I was working in the equally large clinic of the Massachusetts General Hospital. Dr. Legg, always the kindest of men, did the testing at the Carney Hospital. We agreed to test the comparative strength of these two groups of muscles in four different types of feet: symptomless feet, which exhibited, in shoe wear and in walking, normal weight-bearing lines; feet that were symptomless but in which a slight sag toward the inner side (what is usually called pronation) was exhibited; feet that tired easily and were usually tender to pressure beneath the calcaneoscaphoid ligaments and frequently exhibited calluses beneath the anterior arches — this group showed still more faulty lines of weight bearing than those of the second type, that is, more exaggerated pronation; and painful feet, usually but by no means always flat, which were tender to plantar pressure and flexible to passive motion, and were covered by shoes that bulged on their inner sides — these are commonly called "acute flat feet," and their possessors seem to have lost the joy of life.

Dr. Legg and I agreed not to discuss or compare our findings until we had tested a sufficient number of feet to give some reliability to our statistics. When a total of a hundred and twenty tests had been made, including all the four classifications, we compared our figures. To our surprise and satisfaction, we discovered that the averages that we had independently computed in the two different clinics were well-nigh identical. The exact fractional percentages of the different groups were published in 1908.[2]

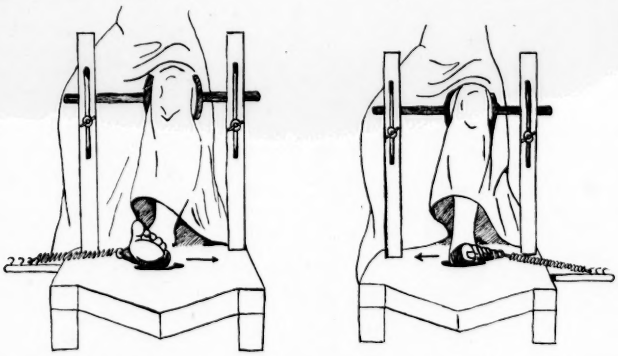

FIGURE 6. *Apparatus for Testing the Strength of the Adductors and Abductors of the Foot.*

In the first group, which one may call the symptomless normal feet, the inverters of the foot, acting as protectors of the arches, were stronger than the everters or depressors of the arches in the ratio of approximately 5 pounds pull of the inverting protectors to 4 pounds pull of the everting depressors.

In the second group, also symptomless but exhibiting slight pronation, the pull of the two groups of muscles was approximately equal, but slightly in favor of the everters or depressors of the arches.

In the third group, that of patients with more pronated feet seeking advice because of symptoms of foot strain, the pounds pull of the everters or depressors of the arches was definitely stronger than that of the inverters or protectors of the arches.

In the fourth group, comprising the "acute flat feet," the ratio of the pounds pull of the inverters to that of the everters was approximately 4:5; in other words, the reverse of the ratio that existed in the test of normal symptomless feet.

On the basis of these tests, it seemed worth while to determine in some impartial manner the possible preventive and therapeutic implications of the findings. An opportunity to examine by means of these muscle tests the feet of probationer nurses was afforded by the superintendent of the School of Nurses at the Massachusetts General Hospital. These young women were taking up an occupation that required longer hours of standing and walking on harder surfaces than the majority of them had experienced. I was informed that in the rather large classes of probationers there had previously been a rough average of one nurse a week obliged to be off duty because of foot strain. For a year, I was allowed to examine and test in the manner I have described the feet of all the probationers soon after they took up their new duties, and to advise them in accordance with the findings of the test. If my memory is honest, no nurse who had followed the advice given on the basis of the test was laid up for foot strain during the year. Moreover, only one of the probationers who exhibited a normal balance test at her original examination reported for foot strain, and her condition proved later to be arthritic and not static. This seemed a little too good to be true, and I asked my colleague, Dr. Lloyd T. Brown, to repeat the clinical experiment the following year. He had the same good luck. The result had been economical for the hospital.

It seemed worth while to attempt to gain an impression of the incidence of faulty muscle balance in otherwise healthy young people. Through the kindness of Miss Amy Homans, then professor of physical culture at Wellesley College, and Miss Randall, her assistant, the foot balance of 350 students was tested in the manner described. Faulty balances were found to be three times commoner than normal balances. Incidentally, Miss Randall reported that only a surprisingly small number of college girls were able to take walks of any considerable distance without general and foot fatigue. This was in 1912–1913, and it is to be hoped that the increase in athletics and the more sensible shoes have by now lessened the prevalence of foot strain in the female college students.

If, in the routine examination of a patient with a tired back and weary feet, one finds an abnormal wear of the shoes, indicating pronation, tenderness to pressure over the strained ligaments of the arches, the other classic signs of foot strain and a faulty muscle balance, what should be done? The first thing, in my opinion, is to make the patient understand what these findings mean in terms of his symptoms and the reasons why the measures proposed may be expected to relieve the symptoms that have induced him to seek advice. In my experience, this is time well spent.

As the first measure, one should recommend that shoes be designed on proper lines and of proper fit. One is inclined to inveigh against the modern ready-made shoe. It is true that the vagaries of fashion are responsible for many foot ills (especially the high heels with a small base), but one should pay a tribute to the manufacturers of shoes and the retailers of their products for their remarkable accomplishments. It is possible, except in the presence of fixed deformities, especially of the toes, to find for almost any shape of foot a ready-made shoe that is both nondeforming and comfortable to wear. The detailed and extensive scientific work of Dr. R. Plato Schwartz,[3] professor of orthopedic surgery at the University of Rochester (New York), is worthy of unstinted praise in this connection, as are Professor Arthur Steindler's[4] excellent studies of the pathology of locomotion. The details of the mechanisms of the human gait are being accurately analyzed for the first time.

One should also correct or compensate for any departure from good weight-bearing lines that may be caused by improper body posture.

Moreover, one should make sure that there is no accessory inhibition, such as the lack of flexibility of the foot that is present when the power of dorsiflexion with the knee fully extended is less than a right angle because of contracted calf groups.

Finally, by some means, the normal muscle balance between the inverters or protectors of the

arches and the everters or depressors of the arches should be restored.

Other potential causes of foot strain should not be overlooked because of this emphasis on what I believe to be a neglected and remediable common cause. Fatigue, poor muscle tone after illness, unreasonably long hours of standing or walking on unreasonably hard surfaces, and vicious shoeing may be important etiologic factors. Overweight is often blamed, but in my experience the muscles usually develop in consonance with the gradual addition of weight if activity is maintained. The association of overweight, a sedentary life and foot strain was known in Biblical times, for in *II Samuel* (IX:13), we read, "So Mephibosheth dwelt in Jerusalem: for he did eat continually at the king's table; and was lame on both his feet."

How can a faulty muscle balance be changed into a normal one? "Aye there's the rub," for it entails exercises persistently followed and precisely performed. Most patients still expect a pill to cure their ills; almost as many pin their faith to an injection. A small number are willing to be massaged and exercised if the physical therapist does most of the work. Work on the patients' part is considered a personal virtue, although the reward of this virtue is their own betterment. If the explanation of the causes of their discomfort has been clear and convincing, I have found it possible to gain excellent co-operation from the vast majority of patients. The methods employed are those of dogmatism, cajolery and fear — not very idealistic methods, I admit, but productive of results.

I insist that patients take only one exercise, which is illustrated by the physician at the time of the visit. They are then presented with a carefully typewritten description of the exercise and four attractively colored marbles. The law of gradual increase in exercise is dogmatically laid down.

The patients are told that they must do these exercises between bed and breakfast, because muscles increase in strength only when they are rested before being exercised and have a chance to rest after being exercised. I remind them that the old adage still holds, "It is no use to whip tired horses," that although it is easier to do stupid exercises just before going to bed, it takes more "guts" when they are sleepy in the morning; if they go to bed without doing the exercises and get up that much earlier in the morning, their total sleeping time is no less and their muscular benefit much greater.

I inculcate fear by telling them that at the next visit — in two or three weeks — I shall be able to tell by the balance test whether or not they have followed the instructions given. It has surprised me much to find how valuable an incentive to struggle such a fear of discovery of not having played the game often is.

The ready-made artificial foot supports commonly known as "foot plates" or "arch supporters," which stores and druggists carry, are, by and large, as much an abomination as one would expect a ready-made set of artificial teeth to be; but if intelligently fitted, such supports are often pain relievers, without having, as a rule, any curative value. I try to distribute the weight appropriately to the individual foot that needs a temporary support by making plaster casts, which are subsequently shaped to attain the desired end and from which light spring-steel or sponge-rubber supports are fashioned. I almost never make heavy or rigid foot supports, which tend to atrophy the intrinsic foot muscles. The type that is recommended for all but the rigid or very heavy or indolent patients provides a light springy support, which relieves the symptoms and holds the arches in position while the patients are attaining and learning how to maintain a normal muscle balance. Once this has been achieved and persevered in, artificial supports become unnecessary, and on any reasonably soft surface, weight bearing becomes a joy. One may even whisper the word "cure."

There have been very few disciples of this method of examination and therapy, although I have continued to employ it for over thirty years and still believe in its soundness. The fact that it is rarely used suggests very strongly that it is of little value, and yet I am somewhat comforted by the remembrance that Thomas's ring-hip splint remained almost unknown or at least unused except by him and a few colleagues for fifty years. But when his nephew, Sir Robert Jones, persuaded Sir Henry Gray, chief surgeon of the Third British Army, to order it applied to all the compound fractures of the thigh on the field before transportation to base hospitals, the mortality from this very common injury dropped from over 80 to 15 per cent. The Medical Department of the United States Army learned how to use this splint before casualties began, and it was the routine treatment prescribed throughout the course of the American Expeditionary Force. It proved an equal lifesaver for our soldiers. Today, all good ambulances are equipped with this almost forgotten splint or its modifications. "Splint 'em where they lie" is still a good slogan. It may be gathered that I think "Balance 'em where they stand" is another. Here is no thought of saving life but of enabling certain people to tread their measures with greater happiness and more comfort.

372 Marlborough Street

References

1. Duchenne, G. B. A. *Physiologie des mouvements démontrée à l'aide de l'expérimentation électrique et de l'observation clinique, et applicable à l'étude des paralysies et des déformations.* 872 pp. Paris: J. B. Bailliére & Sons, 1867.
2. Osgood, R. B. The comparative strength of the adductor and abductor groups in the foot. *Am. J. Orthoped. Surg.* 5:298-303, 1908.
3. Schwartz, R. P., and Heath, A. L. Some factors which influence the balance of the foot in walking. *J. Bone & Joint Surg.* 19:431-442, 1937.
4. Steindler, A. *Mechanics of Normal and Pathological Locomotion in Man.* 424 pp. Springfield: Charles C Thomas, 1935.

DISCUSSION

DR. FRANK R. OBER (Boston): Dr. Osgood has demonstrated a very simple and excellent method for testing the basic difficulty in foot strain — that is, muscular weakness. I agree with him that the term "flat foot" is a bad one. The average person who has a flat foot hardly ever has any trouble with his foot, because the shoe that is bought in the market fits a flat foot and no other foot; therefore, this person is always protected.

Painful symptoms may occur in any type of foot — a flat foot, a highly arched foot or a moderately arched foot. The highly arched foot is the one that gives the most difficulty, however.

The patient should be examined sitting as well as standing. No satisfactory examination of the feet can be made in the standing position alone. A patient may pronate in the standing position and be labeled with a diagnosis of "flat foot," whereas, when the foot is examined in the sitting position, the arch may be much higher. This type of foot is not a flat foot. The feet flatten out on standing because the patient has short posterior calf muscles, and to get the heel down on the floor, the front of the foot must go somewhere and usually goes into the abducted position, causing the ankle to roll inward. If the patient is asked to stand on tiptoe, it will be noticed that his arch is restored to the normal position. However, if a patient has worn flat shoes for years, the medial ligaments become stretched out, so that it is impossible for the patient to support his foot in the normal position, even with the assistance of the muscles.

There have been various attempts to legislate the heights of heels. One may as well try to legislate window glass for spectacles, because no two feet are alike.

According to a certain insurance company, growing pains in children are due to rheumatism. The fact of the matter is that 999 out of 1000 cases are due to foot strain. The patient with a strong foot can wear any type of shoe, but if this patient is sick in bed for two or three months or has some debilitating disease, even his foot will go to pieces when weight is put on it. Patients with short heel cords are much better off with a shoe that has a heel high enough to compensate for the loss of dorsiflexion.

Exercises should be simplified as much as possible, since most people object to doing many. One exercise that uses practically all the muscles of the foot is much more satisfactory. In this exercise, the patient is asked to curl his toes downward and at the same time to invert and dorsiflex his foot. This exercise affects the plantar muscles of the foot, the toe flexors and the anterior and posterior tibial muscles, all of which are the main support of the arch.

The main trouble with the whole shoe situation is that shoes are manufactured on a mass-production basis. Since no two feet are alike in a single person, it is out of the question to expect such a shoe to fit all types of feet. However, if a shank could be made to go into the shoe that could be adjusted to fit the foot, this problem would be solved.

The foot-muscle testing apparatus that Dr. Osgood has discussed is a simple device, not only in checking the weakness in foot muscles but also in checking, from time to time, how well and how faithfully the exercises are being carried out.

DR. OSGOOD (closing): I agree with everything Dr. Ober has said, but the object I have been trying to emphasize is to get rid of the necessity of artificial supports. I am convinced that it is possible to do so in a great many cases. One method of doing it is to test the protectors against the depressors, and then, if the balance is wrong and the depressors are stronger, as they very often are, and if the patient co-operates, the strength of the protectors can be built until a normal muscular mechanism is attained.

It is rather good fun to be able to wear sneakers once in a while, and it is still a pleasure to play tennis. One cannot do that without normal muscle protection.

After what Dr. Ober has said about ready-made shoes, I think I should say something in defense of the shoe manufacturer, because it is remarkable that so few of us have to have our shoes made for us. If we select carefully, most of us can find a shoe that fits reasonably well and, with a normal balance, can escape foot strain.

TOXIC EFFECTS FROM THE INTRAPERITONEAL USE OF SULFANILAMIDE*

Report of Two Cases

MARK FALCON LESSES, M.D.,† AND ARNOLD STARR, M.D.‡

BOSTON

THE use of sulfanilamide as a local therapeutic agent for the prevention or treatment of peritonitis has recently been widely advocated.[1-5] Although the available reports attest its value, little mention is made of toxic effects such as those so frequently described following the oral administration of this drug.[6] Because of the desire to attain a high local concentration, the amounts used intraperitoneally (8 to 15 gm.) have been large when compared with the amounts given in single doses either by mouth or by vein. Extremely rapid absorption from the peritoneum occurs, with resultant high blood levels of sulfanilamide that are soon followed by a drop to low values, a decline probably due to quick disappearance of the drug from the peritoneal cavity. According to most observers, the blood sulfanilamide level is elevated for about forty-eight hours, the highest peak being reached within two to twelve hours.

Toxic effects from the rapid absorption of the massive doses usually employed might therefore be anticipated even more frequently than following its use by mouth. Yet Thompson, Brabson and Walker[4] observed in 59 cases of acute appendicitis treated with intra-abdominal sulfanilamide that no toxic reactions beyond cyanosis occurred, except for 1 case of jaundice, which they attributed to an associated streptococcal peritonitis. On the other hand, Jackson and Coller,[7] although they note the beneficial results of intraperitoneal sulfanilamide therapy in peritonitis, draw attention to the higher incidence of jaundice in these patients as contrasted with those who have received the drug only by mouth. Icterus developed in 6 out of 25 patients who received intraperitoneal sulfanilamide; they attributed the icterus to liver damage.

Two cases are herewith reported in which 8.0 and 12.0 gm. of sulfanilamide were employed intraperitoneally, with resultant toxic reactions in the form of anemia and leukopenia in one case, and anemia and hepatitis in the other.

CASE REPORTS

CASE 1.§ A 62-year-old woman entered the Beth Israel Hospital on February 27, 1941, with the complaint of abdominal pain. She had been well until 2 years previously, when she developed abdominal colic that gradually increased in severity. Three months before admission, she noted pain in the left upper quadrant following meals, as well as gaseous eructations and a feeling of distention. During this same period, the patient became constipated, and there were occasional episodes of rectal bleeding. She had lost 32 pounds in weight in the 4 months preceding admission. Concomitantly, there was pallor of the skin and exertional dyspnea. A roentgenray examination of the large bowel at another hospital was interpreted as showing carcinoma of the colon. The past, family and marital histories were noncontributory.

The positive findings on physical examination were moderate pallor of the skin, conjunctivas and mucous membranes, and a blood pressure of 150/85. The rest of the physical examination revealed no important deviations from the normal.

The urine was free of albumin, sugar, bile or abnormalities of the sediment. The blood showed a red-cell count of 3,250,000 with a hemoglobin of 40 per cent (Sahli), and a white-cell count of 6600, with 71 per cent neutrophils, 20 per cent lymphocytes, 8 per cent monocytes, and 1 per cent basophils. There was slight achromia of the red cells, with moderate variation in the size and shape of the cells, and occasional polychromatophilia; the platelets appeared normal in number. The blood nonprotein nitrogen was 27 mg. and the total protein was 4.9 gm. per 100 cc., with an albumin of 3.04 gm. and a globulin of 1.94 gm.

For 5 days, the patient was prepared for operation with enemas, saline laxatives, intravenous glucose and saline solutions, and a low-residue diet. A transfusion of 500 cc. of citrated whole blood was given the day before operation, without undue reaction. Following transfusion, the red-cell count was 4,590,000 with a hemoglobin of 64 per cent (Sahli), and the white-cell count was 13,800 with 92 per cent neutrophils, 6 per cent lymphocytes and 2 per cent monocytes; there was slight achromia, anisocytosis and poikilocytosis of the red cells.

On the 5th hospital day, laparotomy was performed under spinal anesthesia. A malignant lesion involving the hepatic flexure of the colon was found. There was free, cloudy fluid in the peritoneal cavity, with injected and granular loops of small bowel, indicating early peritonitis. A large carcinomatous mass invaded the right retroperitoneal region, and a perforation was present in the ascending colon just below the hepatic flexure, with slight leakage of intestinal contents. Because of the peritonitis, nothing more than a cecostomy was done; this procedure employed a Pezzar catheter, which was brought out through a short oblique incision in the right lower quadrant. Eight grams of sulfanilamide powder was distributed in the peritoneal cavity, especially about the cecostomy area. The incision was closed with mass sutures of silk, and the cecostomy wound was closed with interrupted catgut sutures.

Following operation, the temperature rose abruptly to about 103°F., and the pulse rate to 120. Pyrexia and

*From the Medical and Surgical services, Beth Israel Hospital.

†Instructor in medicine, Tufts College Medical School; associate visiting physician, Beth Israel Hospital.

‡Instructor in surgery, Tufts College Medical School; junior visiting surgeon, Beth Israel Hospital.

§We are indebted to Dr. Adolph Meltzer for permission to report this case.

tachycardia were maintained at or above these figures until death. Five hours after operation, the blood sulfanilamide level was 12.6 mg. per 100 cc. A sharp drop in the red and white cells of the blood was present (Table 1), with a moderate drop in the hemoglobin but without relative neutropenia. On the day following operation, there was a further drop in the hemoglobin to 46 per cent (Sahli). The red-cell count remained about 2,500,000, and there was further leukopenia, the white-cell count being 2700, with abundant granulocytes. The patient's condition rapidly declined, and death occurred 36 hours after operation. On the day of death, the non-protein nitrogen of the blood was 41 mg. and the total protein was 3.9 gm. per 100 cc. The blood sulfanilamide reading on the morning of death was 7.5 mg. per 100 cc. Later that day, — several hours before death, — the patient was given 4.0 gm. of sulfanilamide intravenously and a transfusion of 500 cc. of citrated whole blood.

TABLE 1. *Laboratory Data in Case 1.*

DATE	RED-CELL COUNT	HEMOGLOBIN (SAHLI)	WHITE-CELL COUNT	POLYMORPHONUCLEARS	LYMPHOCYTES	MONOCYTES	BASOPHILS	BLOOD SULFANILAMIDE
	$\times 10^6$	%	$\times 10^3$	%	%	%	%	*mg./100 cc.*
At admission	3.25	46	6.5	71	20	8	1	
After transfusion	4.59	64	13.8	92	6	2		
Five hours postoperative	2.60	54	4.3	82	12	6		12.6
Twenty-four hours postoperative	2.50	46	2.7	72	16			7.5

Autopsy. At post-mortem examination, jaundice was absent, but the presence of pallor of the mucous membranes, which had been noted clinically, was confirmed.

There were inflammatory changes in the parietal peritoneum extending into the right pelvis and to the viscera contiguous with the anterior abdominal wall. One hundred cubic centimeters of reddish-brown, purulent, foul-smelling material was noted in the abdomen, situated between coils of bowel and in the pelvis. A carcinomatous mass adherent to all adjacent structures was present in the ascending colon just above the cecum.

There were congestion and edema of the lower lobes of both lungs.

The mucosa of the lower two thirds of the esophagus was red and injected, and showed numerous small, dilated submucosal vessels, with small patches of gross hemorrhage in some areas, and diffuse submucosal hemorrhage in others. The mucosa and muscularis of the esophagus were, however, intact throughout. There was marked dilatation of the esophagus, which contained a considerable amount of brown, foul-smelling fluid, similar to that observed in the stomach.

The stomach was of normal size and contained a considerable quantity of fluid similar to that noted in the esophagus. The entire mucosa was covered by a reddish mucoid exudate, and presented beneath its surface numerous areas of submucosal hemorrhage and many small dilated vessels. These gave an appearance of diffuse hemorrhage covering the lower two thirds of the mucosa of the stomach.

The duodenum presented the same appearance, so far as hemorrhage was concerned, as the gastric esophageal mucosa, but these areas were less marked and lighter in color. There was involvement of the muscularis of the third portion of the duodenum by the primary tumor, but no break through the mucosa. There was no evidence of ulcer, tumor or hemorrhage in the small intestine.

Surrounding the cecostomy wound in the colon was a small amount of purulent, fecal-smelling material. There was a 1.5-cm. perforation in the ascending colon, from which fecal material could be freely expressed into the peritoneal cavity. Within the ascending colon was a necrotic papillary tumor, 4.0 cm. in width, completely encircling the bowel and extending above and below the papillary projections. The retroperitoneal tissues of the right lumbar gutter showed marked inflammatory changes, without free pus. No gross hemorrhage was evident. The tumor extended upward to the hepatic flexure, adhered to the head of the pancreas and was slightly fixed to the lower pole of the right kidney, extending to the root of the mesentery of the small intestine, where several lymph nodes were involved. The liver weighed 1740 gm. and was of normal size, shape and consistence. The right lobe was adherent to the tumor mass.

On microscopic examination, some of the bronchioles showed a moderate infiltration of leukocytes and lymphocytes in the fibrous tissue comprising the submucosal layer. The alveoli of the lower lobes appeared compressed and contained small scattered collections of polymorphonuclear leukocytes without fibrin between them. There was marked compression of the alveoli of the lower portion of the lower lobe.

The liver cells showed no degenerative changes. No metastases were present.

The submucosa of the stomach contained numerous blood vessels markedly distended with blood but without free hemorrhage. The same picture was seen in the duodenum.

The primary tumor in the colon was a relatively anaplastic adenocarcinoma. The regional lymph nodes were involved by metastases.

Bone marrow from a rib was moderately cellular and contained, predominantly, cells of the granulocytic series. A moderate number of megakaryocytes were seen, but nucleated red blood cells were rare. The marrow contained a considerable amount of fat but no appreciable amount of fibrous tissue. No metastatic tumor formation was present.

Post-mortem bacteriologic cultures from the heart's blood showed the presence of nonhemolytic streptococci and *Escherichia coli*, whereas cultures from the abdominal fluid contained the same organisms in addition to *Clostridium welchii*.

The patient died of a blood-stream infection, with nonhemolytic streptococci and *Esch. coli*, and generalized peritonitis caused by a perforation into the peritoneal cavity at the site of the adenocarcinoma of the ascending colon. The anemia evidenced by this patient before death was associated with hypoplasia of the red-cell elements of the bone marrow. The hemorrhagic lesions in the intestinal tract were terminal.

Comment. In this case, death was primarily due to septicemia and peritonitis from carcinomatous perforation of the colon, but the development of marked anemia and leukopenia within 5 hours after laparotomy and intraperitoneal instillation of 8.0 gm. of sulfanilamide must be ascribed to the toxic action of this drug. The bone

marrow was hypoplastic in red-cell elements. Although some of this hypoplasia undoubtedly antedated operation, the peripheral blood changes indicated that further depression occurred following the use of sulfanilamide. The marrow showed abundant cells of the granulocytic series, and this too was reflected in the blood stream in the maintenance of an adequate percentage of neutrophils. However, the white blood cells and the absolute number of neutrophils progressively declined, indicating failure of delivery of these cells to the blood stream from the marrow. Other possible mechanisms of blood destruction or blood loss were not operative since the septicemia was caused by nonhemolytic streptococci and *Esch. coli*, and sediment. The blood nonprotein nitrogen was 26 mg. per 100 cc., and the icteric index 9.

Several hours after admission, laparotomy was performed under spinal anesthesia. The peritoneal cavity was filled with turbid brown fluid, which was aspirated and subsequently found to contain *Esch. coli*. An adherent cystic mass, 20 cm. in diameter, arising from the right ovary filled the pelvis. Its wall was congested and necrotic in patchy areas, and purulent fluid oozed from several perforations. The cyst was freed and removed. Its bed contained a mass of greenish-gray membranous tissue resembling the wall of an abscess. In view of the extensive nature of the infection, 12 gm. of

TABLE 2. *Laboratory Data in Case 2.*

DATE	RED-CELL COUNT	HEMOGLOBIN (SAHLI)	WHITE-CELL COUNT	POLYMORPHONUCLEARS	LYMPHOCYTES	MONOCYTES	ICTERIC INDEX	BLOOD SULFANILAMIDE	URINE BILIRUBIN
	$\times 10^6$	%	$\times 10^3$	%	%	%		mg./100 cc.	
2/15*		96	8.6	73	19	6	9		0
2/16†	3.70	68	15.1	94	4	2	9	4.5	0
2/17	3.10	64	14.2	91	7	0	35	7.0	0
2/18	4.20	65	15.4	93	6	2	30		++++
2/19	3.64	66	11.9	91	8	1	25		
2/20	3.30	66	13.2	86	11	1	18	Trace	+++
2/21	3.35	72	10.6	76	18	4	18	0.0	+++
2/24‡	3.60	78	23.7	83	9	7	15		0
2/26	4.10	70	26.8	83	16	1			0
2/27	3.75	72	13.9				13		
3/1	3.75	74	15.4	79	10	8	8		0
3/6§	3.25	68	15.3						0
3/10¶	3.74	76	7.7	84	7	5			+
3/12	4.05	76					6		

*Preoperative.

†Postoperative, following 500-cc. transfusion of whole blood and 5.0 gm. sodium sulfathiazole and 6.0 gm. sulfanilamide intravenously.

‡After 500-cc. transfusion of whole blood.

§After posterior colpotomy.

¶After 500-cc. transfusion of whole blood.

the submucosal gastrointestinal hemorrhages were terminal and inadequate to account for the anemia.

Five hours after operation, the blood sulfanilamide level had risen to 12.6 mg. per 100 cc., indicating that rapid absorption had occurred. The patient also received 4.0 gm. of sulfanilamide intravenously, but this was given well after the onset of the anemia and shortly before death, so that it could not have contributed materially to the toxic reaction.

CASE 2. A 40-year-old woman entered the Beth Israel Hospital on February 15, 1941, complaining of right-sided lower abdominal pain of 6 hours' duration. One month prior to entry, there had been an attack of lower-right-quadrant pain, which subsided without treatment but was followed by symptoms of so-called "grippe," from which complete recovery had occurred. Twenty years previously, there had been an operation for disease of the right ovary.

Physical examination showed a dusky pallor of the skin. The temperature was 105°F., and the pulse rate 158. The abdomen was tense, spastic and diffusely tender. Vaginal examination revealed a moderate whitish discharge, no pain on motion of the cervix, and no abnormalities of the vaults. On bimanual examination, a firm, large, tender abdominal mass was felt in the midline, separate from the uterus. The blood pressure was 160/100. The heart was moderately enlarged to the left and regular in rhythm, with a faint, blowing apical systolic murmur. The lungs showed no abnormalities. The remainder of the physical examination was not noteworthy.

The blood showed a hemoglobin of 96 per cent (Sahli) and a white-cell count of 8600. The urine was acid, with a specific gravity of 1.015, and negative for albumin, sugar and bile, with a trace of acetone and with a normal

sulfanilamide was placed in the peritoneal cavity, and the wound was closed without drainage with interrupted silk-mass sutures. An intravenous infusion of 500 cc. of plasma was given during the operation.

After operation, the pulse and temperature persisted at high levels for about 5 days. In the 24 hours subsequent to laparotomy, the following therapy was administered: 2000 cc. of plasma, 500 cc. of citrated whole blood, 6.0 gm. of sulfanilamide intravenously and 5.0 gm. of sodium sulfathiazole intravenously. On the 2nd postoperative day, 2.0 gm. of sulfathiazole was administered by mouth. No additional chemotherapy was used.

Deep jaundice of the skin and mucous membranes developed 36 hours after operation. At the same time, signs of bilateral pneumonia became apparent both by physical and roentgen-ray examinations. Coincident with the appearance of the jaundice, there was a moderate drop in the red-cell count (Table 2) and the development of a marked bilirubinuria. The administration of sulfonamide compounds was immediately stopped, and although blood studies at intervals of 4 hours showed no further hemolysis, a transfusion of 500 cc. of citrated whole blood was given to return the blood to more normal levels. With the cessation of chemotherapy, no further anemia developed, and there was a gradual decline of the icteric index from its high value of 35 on the 2nd postoperative day to normal on the 14th, with disappearance of bilirubin from the urine. The pneumonia gradually subsided, and by the 6th postoperative day, the patient's condition was good, but the temperature had not quite returned to normal. From this time on, the convalescence was complicated by the development of a pelvic abscess, which manifested itself by leukocytosis and pyrexia and, later, by the appearance of a pelvic mass. This was drained through the posterior cul-de-sac on the

22nd postoperative day. A considerable quantity of foul, yellowish-green pus was evacuated from the abscess cavity. Thence onward, recovery quickly ensued, and the patient left the hospital in good health on the 32nd day after entry.

Comment. This patient, critically ill with diffuse peritonitis, recovered following excision of a ruptured, gangrenous ovarian cyst, and the intraperitoneal instillation of 12.0 gm. of sulfanilamide. However, jaundice and anemia developed as a toxic reaction. The intensity and duration of the bilirubinuria indicated that the jaundice was primarily due to toxic hepatitis, for the moderate hemolysis of the blood could have contributed only a small amount of the increased bilirubin. The blood sulfanilamide level rose to 4.5 mg. per 100 cc. on the morning following operation, and to 7.0 mg. per 100 cc. on the next day, with complete disappearance from the blood stream by the 6th postoperative day.*

Discussion

During the past year, the value of the intraperitoneal use of sulfanilamide in peritonitis has been stressed by several authors, with emphasis on the lack of toxic reactions. Jackson and Coller,[7] however, have already remarked on the increased incidence of jaundice, and the 2 cases herein reported are further evidence of the toxicity of sulfanilamide when given intraperitoneally in large doses. There has been a gradual replacement of sulfanilamide by sulfapyridine, sulfathiazole and other sulfonamide compounds for oral and parenteral therapy, not only because of their greater efficacy but also because of apparent decreased toxicity. The same consideration may well apply to the intraperitoneal application of sulfanilamide, a drug initially selected because of its greater solubility. But this very property causes such rapid absorption that Jackson and Coller believe it doubtful whether the primary local effect lasts more than one or two hours. Throckmorton[8] also found that after six to twelve hours there was no gross evidence of sulfanilamide placed in the peritoneum of rats, in contrast to sulfathiazole, which remained grossly visible for three to six days. This greater solubility not only militates against prolonged local action, but also exposes the entire organism to undesirable reactions. Even the inflamed peritoneum rapidly absorbs sulfanilamide, as is well shown by the speedy elevation of the blood level. Although blood levels are not an index of continued intraperitoneal activity, the peritoneum is such an effective absorbing surface that the duration of local action of a soluble substance like sulfanilamide is necessarily short.

The systemic effect of intraperitoneal sulfanilamide approaches that seen following intravenous administration because of the speed with which high blood levels are reached, and there is probably a more toxic action on the liver than with oral administration because of the site of application. Jackson[9] found a 30 to 40 per cent higher level of sulfanilamide in the portal blood of dogs that had received intraperitoneal sulfanilamide as compared with the level in jugular blood, and suggested that the jaundice might be due to liver damage caused by these high portal levels. In this connection, Bieter and his co-workers[10] have shown in chickens that, even with orally administered sulfonamides, there is selective concentration of sulfanilamide in the liver, as contrasted with sulfapyridine or sulfathiazole.

Goodwin and Findlay,[11] in an experimental investigation of locally applied sulfonamide drugs, pointed out that it is possible to obtain an effective concentration in the blood with locally applied sulfanilamide but not with sulfapyridine or sulfathiazole. The latter substances are removed too slowly from the site of application for any measurable blood concentration to be produced. Throckmorton's[8] experiments on rats, however, indicate that sulfapyridine may be injurious to the peritoneum in contrast to sulfathiazole, which does not cause peritoneal damage and which furthermore has such delayed absorption that the local defense mechanism is augmented by the foreign-body reaction. On the basis of the solubilities and available evidence, therefore, one would be justified in using sulfathiazole rather than sulfanilamide if prolonged intraperitoneal action is desired with minimal general effects.

Summary

Two cases are reported in which the intraperitoneal use of sulfanilamide in massive single doses caused anemia, leukopenia and hepatitis.

The substitution of a less soluble sulfonamide such as sulfathiazole for intraperitoneal use is suggested.

References

1. Herrell, W. E., and Brown, A. E. Local use of sulfonamido compounds in the treatment of infected wounds. *Proc. Staff Meet., Mayo Clin.* 15:611-615, 1940.
2. Mueller, R. S. Use of powdered crystalline sulfanilamide in surgery. *J. A. M. A.* 116:329, 1941.
3. Rosenberg, S., and Wall, N. M. Treatment of diffuse peritonitis by direct intraperitoneal introduction of sulfanilamide. *Surg., Gynec. & Obst.* 72:568-578, 1941.
4. Thompson, J. E., Brabson, J. A., and Walker, J. M. The intra-abdominal application of sulfanilamide in acute appendicitis. *Surg., Gynec. & Obst.* 72:722-727, 1941.
5. Long, L. W., and Dees, J. G. Local use of sulfanilamide. *Surgery* 9:878-882, 1941.
6. Long, P. H., Haviland, J. W., Edwards, L. B., and Bliss, E. A. Toxic manifestations of sulfanilamide and its derivatives, with reference to their importance in course of therapy. *J. A. M. A.* 115:364-368, 1940.
7. Jackson, H. C., and Coller, F. A. The use of sulfanilamide in the peritoneum. *Program of the American Medical Association*, Cleveland, Ohio, June 2-6, 1941. P. 51.
8. Throckmorton, T. D. The peritoneal response to powdered sulfonamide compounds: experimental studies. *Proc. Staff Meet., Mayo Clin.* 16:423-425, 1941.
9. Jackson, H. C. Intraperitoneal sulfanilamide. *Ann. Surg.* 113:1069, 1941.
10. Bieter, R. N., Baker, A. B., Beaton, J. G., Shaffer, J. M., Seery, T. M., and Orr, B. A. Nervous injury produced by sulfanilamide and some of its derivatives in the chicken. Preliminary report. *J. A. M. A.* 116:2231-2236, 1941.
11. Goodwin, L. G., and Findlay, G. M. Absorption and excretion of sulphonamides applied locally: observations in rabbits. *Lancet* 1:691, 1941.

*The 6.0 gm. of sulfanilamide that this patient received intravenously during the twenty-four hours subsequent to operation may well have contributed to the toxic hepatitis, but was probably not the precipitating factor. This is borne out by the short interval between the intravenously administered drug and the onset of the jaundice, and by the low incidence of hepatitis (0.6 per cent in a series of 1000 cases, as reported by Long et al.[6]) following the usual modes of administering sulfanilamide.

CLINICAL NOTE

TREATMENT OF TRICHOMONAL VAGINITIS WITH ACETARSONE TAMPONS

JOE V. MEIGS, M.D.*

BOSTON

IN 1933, Gellhorn[1] advocated the use of acetarsone (Stovarsol) in a powder blower for the treatment of vaginitis due to *Trichomonas vaginalis*. His results were superior to any he had obtained by other methods. Acetarsone is an arsenical and as such may be considered moderately dangerous, but no untoward results were present in Gellhorn's series.

This treatment is usually given in the physician's office and necessitates frequent visits. Hence, it seemed advisable to devise a means for carrying out the treatment at home. This appeared possible by the use of tampons (Tampax) infiltrated with acetarsone, and arrangements were made with a pharmaceutical house for their preparation. It was hoped that these medical tampons would absorb the discharge and control the infection. Since 1938, a number of patients have been treated by this method.

The tampons† are made up by dusting each with 1½ gr. of acetarsone; in addition, a tablet containing ½ gr. of acetarsone, 2 gr. each of glucose, lactose and boric acid, ½ gr. of starch, ¼ gr. of sodium bicarbonate and 4/10 gr. of tartaric acid is placed on the top of each tampon. The pH of the solution of this tablet is approximately 3.0.

In each case, after the diagnosis had been made by examination of a drop of discharge, diluted with two or three drops of warm water, under the high-dry lens of the microscope, the patient was treated with an acetarsone-powder insufflation and then was given the medicated tampons to use at home. For the first week, the tampons were used every night or were inserted in the morning and removed at night. The latter method prevented the discharge from irritating the vulva while the patient was on her feet. At the end of a week, a warm douche of sodium perborate (one tablespoonful to a quart of warm water) was taken, to remove the accumulated powder. During the next week, the tampons were inserted every other day, and during the following week, they were used every third day, the weekly douches being repeated. This went on until the next menstrual period. The medicated tampons were used throughout the period, but after it had ceased, the treatment was omitted for a few days and a smear taken during an office visit. If this was positive, the same treatment was repeated. If the smear was negative, the patient was told to use a tampon twice a week, with a sodium perborate douche at the end of the week. If, after the next period, the vagina was still free from the organism, treatment was stopped.

As part of the treatment, patients were advised to wipe the anus after a bowel movement from front to back and not from back to front, for it is possible that *Trich. hominis* may infect the vagina. Furthermore, all patients were advised to wash their hands carefully both before and after going to the toilet. Absolute cleanliness is necessary, since reinfection of the vagina and vulva may result from chance contamination.

Thirty-nine patients were treated. The duration of the infection was a matter of days in some and of months or years in others. Of the 39 patients, 33 were given one series of treatments; 5, two series; and 1, four series. In 19 cases, the treatment was successful, that is, a negative smear that remained negative after two successive menstrual periods was obtained. In 10 cases, negative smears were not obtained but the patients obtained considerable relief of symptoms; in 6, there was a complete failure. In 4 cases, the treatment was successful the first time but the disease recurred. In 4 patients who had been treated by other methods, the tampon treatment was successful.

Of the 39 patients treated, 26 considered the treatment satisfactory, 6 thought that it was not, and 7 were not sure whether it was helpful or not. In no case was any reaction to arsenic noted. In only a few cases was the treatment given up because of the patient's inability to use the tampons; however, the method was seldom used in young girls.

SUMMARY

The use of medicated tampons containing acetarsone (Stovarsol) is a satisfactory method for the home treatment of patients with vaginitis due to *Trichomonas vaginalis*.

Of 39 patients treated in this way during the past three years, 19 were permanently cured and 7 more were symptomatically relieved.

264 Beacon Street

*Instructor in surgery, Harvard Medical School; chief of Gynecologic Service, Massachusetts General Hospital.

†The medicated tampons are manufactured by the Allen Laboratories, Incorporated, New Brunswick, New Jersey, and are marketed under the trade name, Allen Brand of Tampons with Acetarsone (Stovarsol).

REFERENCE

1. Gellhorn, G. The treatment of trichomonas vaginitis with acetarsone (Stovarsol). *J. A. M. A.* 100:1765, 1933.

MEDICAL PROGRESS

NUTRITIONAL DEFICIENCIES IN RELATION TO THE DIGESTIVE TRACT

CHESTER M. JONES, M.D.*

BOSTON

WITH the realization that specific food substances may affect in a striking manner the production of such diseases as scurvy, rickets, pernicious anemia and similar conditions, much of the investigative work of recent years has concerned itself with an attempt to clarify the action of specific nutritive components on tissue and organic function. The availability of various specific vitamins has further led to numerous observations on the effects of these substances on individual diseases, such as pellagra, and on the manifestations of more general pathologic conditions. Because, in specific deficiency states, almost miraculous clinical changes may be obtained by the use of replacement therapy, there has been a natural, although poorly directed, application of these results to a large number of conditions without critical or well-controlled studies. Such therapeutic enthusiasm, although understandable, is to be regretted because much of it involves wishful thinking and leads to needless and frequently useless forms of therapy at moderate or great expense to the patient. It is pertinent, therefore, to present a few of the numerous studies on the relation between specific nutritional factors and digestive-tract function that have been made by various observers.

As Youmans[1] has been careful to point out, there is very little scientific evidence of the exact effect that vitamin deficiencies exert on disease, and hence little justification for much of the widespread use of vitamins as therapeutic agents in a great number of illnesses. As he states, there is good reason to believe that vitamin deficiencies do occur as complications of many diseases and modify unfavorably their course and outcome. For the present, however, the influence of vitamin deficiencies must be considered to be that which might reasonably be expected from poor general nutrition. There is little reason to doubt that mild or subclinical pellagra has an effect on the course of other illnesses, but no specific information is as yet available of the exact effect that such a deficiency produces. The fact that no good clinical test for most hypovitaminoses exists gives most deductions a speculative rather than a truly scientific value.

Further limitations to the value of clinical or animal investigations are obvious when one remembers, as Spies and his group[2] point out, that vitamin B, which was formerly considered a single substance, is probably composed of twelve or more separate factors, each of which together with unknown substances contributes to the total effect of various therapeutic agents, such as yeast, wheat germ and liver extract. The wisdom of general replacement therapy is borne out by his experiences at the Hillman Hospital, where studies were made on a group of 1250 consecutive cases of malnutrition. In addition to specific vitamin lacks, it was noted, for example, that a large number of persons received as little as 50 per cent of the estimated energy requirements, and in many cases the protein intake was too low to maintain nitrogen equilibrium. Nearly all the patients received substandard amounts of calcium, phosphorus and iron, and none obtained standard amounts of all three elements. Spies and his collaborators stressed the value of administering water-soluble and fat-soluble vitamins together, rather than as individual prescriptions, as the most useful method of treating most deficiencies. Mackie et al.,[3] in an excellent review of vitamin deficiency in gastrointestinal disease, stress the point that symptoms may be produced because of certain disturbances of normal body chemistry due to avitaminosis without demonstrable clinical evidence of disease except in a few cases. They also point out the frequently forgotten fact that many of the dietary regimes in vogue for the treatment of diseases of the digestive system are open to grave suspicion so far as adequacy of food constituents is concerned. A practical consideration of some of the causes leading to avitaminosis is indicated in a paper by Rosenblum and Jolliffe,[4] who observe that various therapeutic maneuvers very definitely contribute to vitamin lack or interfere with the normal utilization of the vitamins that are being administered. In the presence of alkali therapy, orally administered ascorbic acid, thiamin chloride, riboflavin and perhaps other vitamins are inactivated or destroyed. Absorption of large amounts of these and other vitamins may be associated with the use of col-

Reprints of articles in this series are not available for distribution, but the articles will be published in book form. The current volume is *Medical Progress: Annual, 1940* (Springfield, Illinois: Charles C Thomas Company, 1941. $4.00).

*Clinical professor of medicine, Harvard Medical School; physician, Massachusetts General Hospital.

loidal aluminum hydroxide or of magnesium trisilicate. Oral treatment with the fat-soluble vitamins may definitely be adversely affected by the associated ingestion of liquid petrolatum. From the surgical aspect, a too liberal use of fluids parenterally, in the form of glucose solutions, contributes distinctly to the increased elimination of members of the vitamin B complex, and is particularly undesirable when operative procedures on the gastrointestinal tract have been performed. A similar danger prevails in other states in which parenteral feeding is necessary.

Numerous references to the effect of already existing gastrointestinal disease on the production of dietary deficiencies are to be found. Brown,[5] along with many others, mentions the occurrence of various deficiency states secondary to prolonged vomiting, diarrhea and the like. In addition, he is authority for the statement, which is probably correct, that actual ulcerative disease of the colon may occur as the aftermath of a poorly balanced diet, particularly when associated with unusual stress, such as intercurrent infection or pregnancy. He mentions the finding of frank ulcerations of the colon resulting from such conditions. Exact proof for such statements is still lacking, but there can be no doubt that at times profound organic changes occur at different levels of the digestive tract as the result of general or specific malnutrition. Bean and Spies[6] mention their findings in 100 persons studied in an area of endemic pellagra, beriberi and riboflavin deficiency, who developed such symptoms as a complication of chronic diarrhea. They also note that chronic diarrhea itself predisposes to the development of deficiency syndromes because of increased loss of nutritive products and decreased absorption, and they also point out that if the diarrhea is relieved, even without vitamin therapy the secondary deficiency is usually improved. In their article, these authors advocate, as many others do, the use of parenteral injections of crystalline vitamins in the presence of active diarrhea because these substances are lost when given orally. They insist, however, that in most cases parenterally given vitamin preparations do not take the place of a high-protein, high-calorie diet, together with large doses of nicotinic acid, thiamin hydrochloride and riboflavin. They suggest the daily use of between 500 and 1000 mg. of nicotinic acid amid, 10 to 50 mg. of thiamin hydrochloride, and 2 to 10 mg. of riboflavin during the acute manifestations of deficiency.

Among the objective changes in the alimentary tract that are properly attributed to avitaminosis, Wilbur[7] mentions the symptoms of anorexia and diarrhea, abnormalities in function, such as achlorhydria, alterations of the motor and absorptive activities of the intestine, and such lesions as stomatitis, glossitis, proctitis, and atrophy and inflammation of the gastric and intestinal mucosa. Although proof of the exact etiology of any or all of these changes is still incomplete, he quite rightly stresses the benefit of careful inspection of the oral cavity, analysis of gastric contents, x-ray films of the alimentary tract with particular reference to the small intestine, and other searches for vitamin deficiency, such as the demonstration of peripheral neuritis, edema and night blindness. These conceptions are not new but are worthy of repetition.

That the function of the bowel is seriously interfered with in the presence of deficiency disease has been noted by various observers. For example, Groen[8] has shown that the absorption of glucose from the small intestine is distinctly interfered with in various deficiency conditions and can be restored to normal by proper replacement therapy. Similarly, Beams, Free and Glenn,[9] in studying patients with pellagra and nontropical sprue, found impaired absorption of galactose, with improvement, at least in patients suffering from pellagra, following specific therapy. They also noted that several cases of rosacea keratitis, which responded to riboflavin therapy, gave indication of increased galactose absorption that later improved, with the disappearance of the skin lesions.

Changes in the gastric mucosa in numerous deficiency diseases have been mentioned by various investigators and need only be noted briefly to indicate the effect of such a change in rounding out the vicious circle of malnutrition. X-ray evidences of disturbed motor or absorptive function in the small bowel have been noted by numerous investigators in patients suffering from various forms of dietary lack. These changes, for the most part, are in association with diarrheal states and are demonstrable as changes in tone, caliber and motility of the small bowel or as complete disappearance of the distinctive mucosal markings. Evidence has been produced that they may be effected by protein deficiency or by lack of various members of the B complex. A too exact interpretation of the x-ray findings mentioned by Kantor,[10] Mackie,[11] Golden,[12] Tyler[13] and others should not be attempted at the present time. Perusal of various articles that have appeared in recent years on this particular phase of small-bowel disturbance leads to the conclusion that strict deductions about functional or cellular changes in the small bowel, as evidenced by x-ray studies, should be made with extreme caution. That such changes may be seen in idiopathic steatorrhea, advanced ulcerative colitis, tropical sprue, infantile celiac disease, pellagra and other conditions is undoubtedly true. As Mackie properly points out, however, such a "deficiency pattern" may occur in a variety of conditions, such as nephrosis, diabetes

insipidus, diseases of the mesenteric lymphatics, abdominal cancer and certain jaundiced states. He also mentions a most interesting fact, which as yet is unexplained — namely, that the same alterations in mucosal pattern can be observed in the intestine of the normal newborn infant. Since these changes disappear early in life and since degeneration of the nerve cells of the myenteric plexuses in adults presenting the deficiency pattern has been demonstrated, these modifications of the normal mucosal pattern of the small bowel are probably the result of interference with the intrinsic nervous mechanism. Confirmation of such a hypothesis, in my experience, may be found in the histologic demonstration of profound atrophic changes existing in Auerbach's and Meissner's plexuses in patients dying with advanced pellagra. According to Mackie and others, such changes can usually be reversed by the enthusiastic administration of the B complex in the form of crude liver extract and yeast. The more concentrated preparations, as a rule, are less effective or may be ineffective. A detailed description of the radiologic changes in the small bowel supposedly secondary to vitamin B deficiency is given by Golden,[12] but it should be stated that as yet not all radiologists are in entire agreement with this author.

An interesting and moot question is that of the interrelation of deficiency disease and resistance to infection. Riddle, Spies and Hudson[14] have made certain interesting observations on 150 selected cases of pellagra, riboflavin deficiency and beriberi. Before, during and after treatment, the bacterial flora of the lesions associated with various vitamin deficiencies was investigated, and certain immune reactions were studied. The lesions at the corner of the mouth characteristic of riboflavin deficiency were found to contain pure or nearly pure cultures of certain strains of *Staphylococcus aureus* in 80 per cent of the cases, and in the remaining 20 per cent *Streptococcus haemolyticus* predominated. Following the oral or intravenous administration of riboflavin or of substances rich in it, the fissures healed rapidly, and the organisms were no longer demonstrable. A study of the bacterial flora of the conjunctival sacs was made in cases of deficiency disease with associated conjunctivitis, and hemolytic strains of *Staph. aureus* were found to predominate in half of 30 cases. In addition to large numbers of Vincent's organisms, two thirds of the patients showing ulcerations of the tongue, gums or buccal mucosa yielded hemolytic streptococci, and the remaining third showed hemolytic strains of *Staph. aureus*. Following specific therapy with antipellagric substances, the bacterial flora, including the Vincent's organisms, promptly disappeared. Apparently, a low complement titer existed in many of the acutely deficient patients and rose coincidentally with clinical improvement. In the whole blood of acutely deficient patients, there was a distinct depression in the bactericidal power for *Staph. aureus*, but little, if any, diminution was noted in the subclinical or mild cases of deficiency. Chapman and Harris[15] observed that monkeys maintained on certain vitamin-deficient diets developed a tendency to oral lesions accompanied by an increase in the fusospirochetal flora. This was apparently in association with diets deficient in parts of the vitamin B_2 complex. Those animals on an adequate stock diet tended to resist the artificial implants of the fusospirochetal flora under the severest of test conditions. The presence of glossitis, buccal aphthae and similar changes is a well-known accompaniment of various deficiency states, and the response to certain members of the vitamin B complex is now generally recognized. It is still essential, however, to stress the fact that careful observation of the tongue frequently yields a clue to an otherwise subclinical deficiency condition existing in patients requiring surgery of the gastrointestinal tract and may indicate the need for more than average care in the preoperative preparation. The report of Manson-Bahr[16] includes a very complete discussion of glossitis, with particular reference to vitamin B_2 deficiency in pellagra, sprue and allied states. Among other interesting facts, the author mentions a study of 500 cases of tropical sprue seen in India, Burma and other oriental countries. In three fourths of these patients, striking glossitis was one of the most prominent symptoms even when no anemia was observed. Improvement following the use of nicotinic acid was rapid, and corresponded to the results obtained in pellagra and certain other conditions. Manson-Bahr also points out the important consideration that changes in the buccal mucosa and tongue may be the result of nicotinic acid or riboflavin deficiency incident to an underlying pathologic condition.

Numerous studies on individual vitamin requirements and deficiency are of interest. It is generally admitted that the absolute requirements of the various specific food substances are still not known. The work of Elsom and Machella[17] on the intake of thiamin and its relation to other dietary constituents in food selected by normal subjects is of interest. Observations on a small group of normal subjects showed that the average daily intake of thiamin exceeded the theoretical requirement by 40 per cent, but the individual intake ranged from 6 to 115 per cent above the so-called "maintenance need." There was a tremendous variation of thiamin intake on individual days in the

same person. A linear relation existed between the daily intake of protein and that of thiamin, and to a lesser extent, between the fat and thiamin content of the diet. The effect of gastric acidity in protecting against the destruction of thiamin given orally was studied by Melnick, Robinson and Field,[18] and the loss of thiamin resulting from intermixture with bile or pancreatic juice or antacids was noted. The value of administering thiamin together with food appeared to be evident in these studies, since the presence of food in the stomach apparently retained the vitamin for a longer period in that organ and thus avoided possible destruction and permitted more or less absorption directly through the gastric mucosa. Also, the normal acidity of the gastric chyme after the intake of food tended to reduce the pH of the intestinal secretion and therefore to diminish possible loss of the vitamin in the duodenal juices. Borson,[19] in a study of thiamin absorption in man by the thiochrome excretion method, showed that the efficiency of utilization of thiamin supplements depends partly on the degrees of absorption and excretion, large doses orally being incompletely absorbed and large doses parenterally being rapidly excreted, so that small, frequent doses appeared to be the most effective method of administration.

That many of the symptoms attributable to vitamin B_1 deficiency are not particularly distinctive is borne out by the studies of Williams, Mason and Smith,[20] who more or less crystallized the suggestions obtained in other clinical reports following a series of careful observations on 4 young women placed on a diet more deficient in thiamin than is commonly reported in association with beriberi. In the second half of a period of twenty-one weeks on a vitamin B_1 deficient diet, the urinary output fell to an extraordinarily low level, and during this period anorexia, fatigue, loss of weight, absent or a low free-gastric acidity, constipation and inconstant tenderness of the muscles of the calves were noted. Toward the end of the period, there was evidence of a slight impairment of the absorption of glucose. Electrocardiographic abnormalities occurred in all 4 cases. Within twelve days after the parenteral administration of only 4 mg. of thiamin chloride daily, all symptoms and all defects incident to the previous deficiency had disappeared. There is no complete agreement concerning the effect of vitamin B_1 deficiency on gastric function. According to Dyer and Roe,[21] animal experiments indicate that in acute or chronic deficiency there is no abnormal effect on gastric secretory activity, except when the animals are obviously in a moribund condition. The report of Williams et al.[20] suggests that in man this is not so, since a diminution of gastric acidity could be noted as one of the clinical manifestations of vitamin B_1 lack. Dick and Hege[22] found that peristaltic activity of the small bowel in rats was definitely diminished and that loss of tonus in the presence of a dietary lack of vitamin B_1 was evident. Here again, however, exact information is still lacking. It is the impression of Crandall and his collaborators[23] that the pellagra-preventing factor (nicotinic acid, nicotinamide or any carboxypyridine derivative capable of replacing these substances in the diet) is essential to the maintenance of normal gastrointestinal motility. They believe that the absence of this factor leads to motor dysfunction of the intestinal tract but base their opinion largely on the response of many cases of functional digestive disturbance in human beings to nicotinic acid. Additional evidence is found in the abnormal intestinal motility appearing in dogs on a black-tongue-producing diet long before mouth lesions are evident. The authors have not been able to demonstrate any effectiveness of thiamin or riboflavin in functional digestive disturbances, but believe that other factors in the vitamin B_1 complex may be concerned with gastrointestinal motility, in addition to the pellagra-preventing factor.

Evidence of the difficulty in assigning pathologic changes to the lack of a given substance of the vitamin B complex is shown in the report of a necropsy by Nakamura et al.[24] Clinically, the patient developed the classic picture of pellagra and was so diagnosed. Autopsy showed gastric atrophy, numerous hemorrhages in the entire gastrointestinal tract, with round-cell infiltration between the muscle fibers of the pylorus, particularly in the neighborhood of the intrinsic-nerve fibers, and muscle atrophy of the small bowel, with extravasation of blood around the capillaries of the follicles. In addition to the above changes, however, clinical and histologic evidence could be found of peripheral neuritis and myocardial changes usually thought to be associated with thiamin deficiency. Full doses of vitamins B_1 and B_2 had failed to produce clinical improvement. Such a report illustrates the inability to assign exact tissue changes to specific vitamin deficiencies and confirms the fact that single deficiencies are uncommon in man. Additional evidence of the complexity of this problem is given in an article by Spies, Bean and Ashe,[25] who report on a large series of undernourished persons with clinical evidence of pellagra, beriberi and riboflavin deficiency. Some of these patients, in spite of full doses of nicotinic acid, thiamin and riboflavin, continued to have symptoms of extreme nervousness, insomnia, irritability, abdominal pain, weakness and dif-

ficulty in walking. In this group, striking symptomatic improvement was obtained by the addition of large doses of synthetic vitamin B_6. Similarly, Fouts and his co-workers[26] failed to control the anorexia, loss of weight, intermittent diarrhea, moderate anemia and ultimate death in dogs fed on a synthetic diet that contained all the above components of the vitamin B complex in crystalline form, except for a factor or factors contained in a purified liver extract. Still further evidence of the multiple and mixed nature of dietary deficiency disease is suggested by a report of Spies and his group[27] on the action of adenylic acid, which is a constituent of the pyridine dinucleotides and is widely distributed in nature. It is intimately concerned with carbohydrate and protein metabolism. These authors believe that they have evidence that it may act in a manner similar to that of riboflavin in increasing the effectiveness of nicotinic acid. As yet, preparations of adenylic acid for safe parenteral use are not available.

Other studies having particular bearing on the motility of the gastrointestinal tract are those of Martin et al.,[28] who investigated the action of various members of the vitamin B complex on gastrointestinal motility in dogs. They concluded that inositol and nicotinic acid are the members of the vitamin B group directly concerned with gastrointestinal motility. They suggest that the ratio of nicotinic acid or similar compounds to inositol is the nutritional factor determining hypomotility or hypermotility.

An interesting experiment by Elsom and his group[29] is that conducted on a healthy subject who voluntarily went on a constant diet adequate except for vitamin B complex. The symptoms that developed were partially controlled by the administration of thiamin, were influenced very little by the administration of riboflavin, and were relieved by the administration of brewers' yeast. Anorexia was promptly but only temporarily relieved by thiamin, but other evidences of gastrointestinal dysfunction, which included the x-ray demonstration of delayed motility in the small bowel, were not relieved until yeast was added to the diet. Edema of the upper and lower extremities appeared early in the deficiency and was uninfluenced by thiamin or riboflavin, and in spite of the edema, weight loss occurred. Both the edema and the weight loss were corrected only by the administration of yeast. Spies and his collaborators[30] contribute a practical observation regarding the treatment of vitamin B complex deficiency in their study of 23 patients treated by the daily ingestion of a yeast-peanut-butter mixture. Although yeast and peanut butter both contain nicotinic acid, riboflavin and thiamin, the total effect of this supplement to the diet is not due to these vitamins alone, since per unit of weight this compound contains as much carbohydrate as potato, more protein than steak and as much fat as butter.

The probable value of attention to vitamin B complex deficiency in the presence of infection, particularly that involving the gastrointestinal tract, is shown in a report by Aballi and Escobar Aces,[31] who studied this avitaminosis in 63 infants in a Cuban clinic, many of whom had severe enteric infections. In the group with clinical manifestations of vitamin B deficiency, a third of the patients died. In the remainder, adequate oral treatment with various vitamin B concentrates not only cleared up objective manifestations of deficiencies in these substances, but produced rapid improvement in the underlying enteric disturbance.

Sydenstricker,[32] in commenting on the treatment of multiple vitamin deficiencies, is responsible for a significant statement concerning the various components of the vitamin B group — that signs of any one avitaminosis are always indicative of multiple vitamin deficiencies. Therapy with a single component of the vitamin B group, as indicated by pertinent physical signs, may result in the rapid development of severe manifestations of other deficiencies. For this reason, he emphasizes the advantage of administering all other available vitamins in amounts representing at least four to five times the normal daily requirements, in addition to relatively greater amounts of the particular vitamin that is thought to be lacking on the basis of clinical signs.

Because of the facility with which vitamin C determinations may be made on blood and urine, numerous studies have been made bearing on the effects of vitamin C deficiency. The usually accepted optimum intake of this particular vitamin is fairly well established at 100 mg. a day for the average adult in health. Under normal conditions, the absorption of vitamin C from the intestinal tract is nearly complete. Abnormal bowel activity due to disease or catharsis may interfere seriously with the absorption of ascorbic acid, however, and under conditions in which vomiting or diarrhea exists, the parenteral administration is imperative, particularly as a preoperative and postoperative procedure. The amount of vitamin C necessary to "saturate" patients with ulcerative colitis may run to doses as high as 2 to 6 gm., according to Bercovitz.[33] Once saturation has been accomplished, maintenance requirements are obviously definitely increased over the above-noted dosage of about 100 mg. a day. The administration of vitamin C in ulcerative colitis is of benefit because it undoubtedly helps to control one of the major features of the disease — mucosal bleeding.

The relation between vitamin C deficiency and peptic ulcer still continues to be studied. That low plasma levels of ascorbic acid are commonly encountered in patients suffering from peptic ulcer is well known, and there is every reason to believe that this lack is occasioned by dietary restrictions rather than that the vitamin deficiency itself has anything to do with the etiology of gastric or duodenal ulceration. Once established, however, such a deficiency may retard healing, and for this reason, as in other chronic diseases, it is essential to maintain a balanced diet, and the administration of optimum doses of vitamin C may assume real clinical value as a detail in ulcer therapy. The frequency with which vitamin C lack exists in gastric disease is illustrated by the dietary histories obtained by Ludden and his group[34] in a number of patients selected from the gastrointestinal and surgical clinics of the Bellevue Hospital. Dietary histories of this group of patients revealed that voluntary or prescribed diets had been very low in vitamin C. Twenty-three of 28 patients had gastric lesions; of the entire group, 1 had frank clinical scurvy, and 26 had subclinical scurvy, as indicated by laboratory data. In these patients, doses ranging from 1.5 to 11.4 gm., given from three to seventeen days, were necessary to bring about "saturation." A maintenance dosage of as high as 200 mg. daily was needed in a patient with a total gastrectomy, but other patients studied with gastric lesions conformed to the usual accepted maintenance requirements. Field et al.[35] report on their findings in 58 patients with peptic ulcer. They demonstrated in 29 patients that the plasma ascorbic acid values were below 0.5 mg. per 100 cc.; 10 out of 12 who were admitted to the hospital with hemorrhage had values below 0.4 mg. per 100 cc. The authors are probably correct in ascribing significance to the fact that in 2 patients in this latter group, bleeding occurred after they had been maintained on an ulcer regime for eighteen and twenty-six days respectively. Field calls attention to the need for vitamin C therapy as a valuable adjunct in the treatment of peptic ulcer and again stresses the fact that alkali therapy in ulcer patients may contribute to the deficiency in this vitamin and in vitamin B_1. Ingalls and Warren[36] present even more striking figures so far as the actual plasma levels of vitamin C in patients with ulcer are concerned. Eighteen out of 20 patients had low plasma values for this vitamin. Six, whose histories included previous hemorrhages, had blood levels of 0.2 mg. per 100 cc. or less. Further evidence that deficiency diseases are usually multiple is found in the report from the Hillman Hospital[37] on blood and plasma ascorbic acid concentrations in patients with pellagra and associated deficiency diseases. Marked reduction in blood values was found in many of the group studied, and the comment is made that these studies were carried out at a period when leafy vegetables and berries had been available to the patients for some time. In all probability, much greater deficiencies of vitamin C could have been demonstrated in the winter months.

The relation between the fat-soluble vitamins and disturbances of the gastrointestinal tract has been the basis of some studies. The absorption of carotene, the precursor of vitamin A, was studied by means of isolated intestinal loops by Irvin, Kopala and Johnston.[38] In the absence of bile or pancreatic lipase, only insignificant amounts are absorbed in the small bowel, but the addition of either or both of these substances affects absorption materially, and the addition of pure bile salts still further increases the amount of carotene absorbed. Previous reports on the inhibitory effect of mineral oil on the absorption of carotene are confirmed. May and McCreary[39] measured the amount of absorption of vitamin A in infants and children during various stages of celiac disease, or in children with the celiac syndrome secondary to other disorders. A low rise in the level of vitamin A in the vitamin-absorption test was a constant feature of celiac disease, and a similar finding was frequently observed in other conditions simulating this disease. Although not diagnostic of celiac disease, the test for vitamin A absorption described by these authors is helpful in following the clinical progress of recovery from celiac disease, since vitamin A absorption appears to return to normal when cure is complete. The level of blood carotene in celiac disease also seems to follow the clinical course of the disease, being low during the active stage and rising during improvement. Interference with the rise in plasma vitamin A following the ingestion of this substance was also noted by Ralli and his collaborators[40] in patients with liver disease and is in keeping with the finding of a low concentration of the vitamin, as previously noted in cirrhotic livers.

Studies on the effect of vitamin A deficiency on gastric function by Dyer and Roe[41] and by Herrin[42] indicate that lack of this vitamin does not, in animals, diminish the secretory power of the gastric cells or, to any important degree, the motility of the stomach. Some enthusiastic comments on the clinical use of vitamin A, with resulting improvement of gastric secretion in cases of achlorhydria, and more particularly in the successful treatment of peptic ulcer, are to be found in the reports of Földes and Vajda[43] and of Seelig.[44] The studies, although interesting, are far from convincing.

The keratinization of squamous-cell mucous membranes and the proliferation of epithelial cells

have been noted by various investigators of deficiency of this fat-soluble vitamin. The finding of proliferative changes in the columnar cells of the mucosal lining of the stomach in rats by Fridericia et al.[45] in the presence of vitamin A deficiency is therefore of some interest. Of particular significance are the observations that, in their experiments, gastric mucosal lesions occurred in animals kept on alternating deficient and normal diets for many weeks, but that restoration to a normal diet for a year reversed the changes that apparently had taken place in most of the animals. A somewhat similar study by Beck and Peacock[46] demonstrated that animals kept on a vitamin A deficient diet for a year developed ulcerations and papillomatous lesions of the forestomach. No alteration in intestinal permeability to bacterial toxins could be demonstrated, however, by Stryker and Janota[47] in animals on prolonged vitamin A deficiencies.

Abels et al.[48] found low plasma levels for vitamin A in the majority of patients with gastrointestinal cancer, but believed that this could be explained on the basis of an inadequate ingestion and absorption of the vitamin or an associated hepatic dysfunction so far as the storage of vitamin A or its formation from carotene was concerned. The fact that the plasma levels of vitamin A could be increased in these patients by the administration of yeast and lipocaic, which are free of carotenoids, can probably be explained on the basis of the lipotropic action of these substances. It is also possible, however, that these patients presented other deficiencies due to inadequate food intake, and that the administration of yeast resulted, among other things, in better intestinal absorption.

The whole problem of hypovitaminosis of all fat-soluble vitamins caused by steatorrhea is presented in unusually complete form in the report of Albright and Stewart.[49] These authors emphasize the fact that pan-fat-soluble vitamin deficiency should be looked for in all cases of chronic diarrhea, regardless of the presenting symptom, and that when possible these patients should be given fat-soluble vitamins in fat-free vehicles, to obtain maximum dosage and maximum absorption. Such a consideration is of particular value in diseases like ileitis and ulcerative colitis, in which, as Mackie, Albright and others have demonstrated, a prothrombin lack with subsequent spontaneous bleeding may be a major clinical feature. That general nutritional deficiency states may include evidence of vitamin K lack, as well as that of other fat-soluble vitamins, is indicated by the study of Warner, Spies and Owen.[50] Forty-eight patients seen in the nutritional clinic of the Hillman Hospital with evidence of deficiency of one or more of the factors of the vitamin B complex were observed with relation to the prothrombin level and compared with a series of 37 patients on the Medical Service of the Iowa University Medical School. In both groups, moderate hypoprothrombinemia was demonstrated, a higher percentage being found in the patients seen in the northern clinic. The findings did not seem to be the result of vitamin K deficiency, however, in most cases, since large doses of this vitamin did not influence the prothrombin level. It was believed that the subnormal prothrombin production was rather the result of general debility than of nutritional deficiency alone.

* * *

It is obvious that significant additions are being made gradually to information regarding the relation between nutritional disturbance and the function of the digestive tract. In the absence of easily applied clinical tests for avitaminoses and in the presence of many empty spaces in knowledge of the pathologic physiology associated with deficiency disease, it is the part of wisdom to treat any condition of deficiency as one with multiple components by means of those easily available food substances that can be readily obtained and taken orally. In certain cases, parenteral therapy is, of course, indicated, but every attempt should be made to utilize the oral administration of substances such as yeast, adequate amounts of protein and a really well-balanced diet.

References

1. Youmans, J. B. The influence of vitamin deficiencies on other diseases. *Ann. Int. Med.* 13:980-986, 1939.
2. Spies, T. D., Swain, A. P., and Grant, J. M. Clinically associated deficiency diseases. *Am. J. M. Sc.* 200:536-541, 1940.
3. Mackie, T. T., Eddy, W. H., and Mills, M. A. Vitamin deficiencies in gastrointestinal disease. *Ann. Int. Med.* 14:28-41, 1940.
4. Rosenblum, L. A., and Jolliffe, N. The oral manifestations of vitamin deficiencies. *J. A. M. A.* 117:2245-2248, 1941.
5. Brown, P. W. Dietary deficiency in gastro-intestinal diseases. *Mil. Surgeon* 84:375-377, 1939.
6. Bean, W. B., and Spies, T. D. Vitamin deficiencies in diarrheal states. *J. A. M. A.* 115:1078-1081, 1940.
7. Wilbur, D. L. The effects of vitamin deficiency on the gastrointestinal tract. *Am. J. Digest. Dis.* 6:610-617, 1939.
8. Groen, J. The absorption of glucose from the small intestine in deficiency disease. *New Eng. J. Med.* 218:247-253, 1938.
9. Beams, A. J., Free, A. H., and Glenn, P. M. The absorption of galactose from the gastro-intestinal tract in deficiency diseases. *Am. J. Digest. Dis.* 8:415-421, 1941.
10. Kantor, J. L. The roentgen diagnosis of idiopathic steatorrhea and allied conditions: practical value of the "moulage sign." *Am. J. Roentgenol.* 41:758-778, 1939.
11. Mackie, T. T. Vitamin deficiencies and the small intestine. *J. A. M. A.* 117:910-912, 1941.
12. Golden, R. The small intestine in vitamin B deficiency. *J. A. M. A.* 117:913-917, 1941.
13. Tyler, A. F. Study of the small bowel with special reference to avitaminosis. *Nebraska M. J.* 25:441-444, 1940.
14. Riddle, J. W., Spies, T. D., and Hudson, N. P. A note on the interrelationship of deficiency diseases and resistance to infection. *Proc. Soc. Exper. Biol. & Med.* 45:361-364, 1940.
15. Chapman, O. D., and Harris, A. E. Oral lesions associated with dietary deficiencies in monkeys. *J. Infectious Dis.* 69:7-17, 1941.
16. Manson-Bahr, P. H. Glossitis and vitamin B_2 complex in pellagra, sprue and allied states. *Lancet* 2:317-320, 356-359, 1940.
17. Elsom, K. O'S., and Machella, T. E. Studies of the B vitamins in the human subject. I. The intake of thiamine and its relation to other dietary constituents in food selected by the normal subject. *Am. J. M. Sc.* 202:502-512, 1941.

18. Melnick, D., Robinson, W. D., and Field, H., Jr. Fate of thiamine in the digestive secretions. *J. Biol. Chem.* **138**:49-61, 1941.
19. Borson, H. J. Clinical application of the thiochrome reaction in the study of thiamin (vitamin B_1) deficiency. *Ann. Int. Med.* **14**:1-27, 1940.
20. Williams, R. D., Mason, H. L., and Smith, B. F. Induced vitamin B_1 deficiency in human subjects. *Proc. Staff Meet., Mayo Clin.* **14**:787-793, 1939.
21. Dyer, H. M., and Roe, J. H. The relation of nutrition to gastric function. III. The effect of vitamin B_1 deficiency. *Am. J. Digest. Dis.* **8**:329-333, 1941.
22. Dick, M., and Hege, J. R., Jr. The effect of thiamin on the intestine of the B_1-deficient rat. *Am. J. Physiol.* **132**:636-639, 1941.
23. Crandall, L. A., Jr., Chesley, F. F., Hansen, D., and Dunbar, J. The relationship of the P-P factor to gastrointestinal motility. *Proc. Soc. Exper. Biol. & Med.* **41**:472-474, 1939.
24. Nakamura, M., Hamada, C., and Oriuchi, H. Report of necropsy on pellagra. *Bull. Nat. M. A., Japan* **30**:179, 1941.
25. Spies, T. D., Bean, W. B., and Ashe, W. F. A note on the use of vitamin B_6 in human nutrition. *J. A. M. A.* **112**:2414, 1939.
26. Fouts, P. J., Helmer, O. M., and Lepkovsky, S. Factor II deficiency in dogs. *J. Nutrition* **19**:393-400, 1940.
27. Spies, T. D., Bean, W. B., and Vilter, R. W. Adenylic acid in human nutrition. *Ann. Int. Med.* **13**:1616-1618, 1940.
28. Martin, G. J., Thompson, M. R., and de Carvajal-Forero, J. The influence of inositol and other B complex factors upon the motility of the gastro-intestinal tract. *Am. J. Digest. Dis.* **8**:290-295, 1941.
29. Elsom, K. O., Lewy, F. H., and Heublein, G. W. Clinical studies of experimental human vitamin B complex deficiency. *Am. J. M. Sc.* **200**:757-764, 1940.
30. Spies, T. D., Grant, H. M., and Grant, J. M. Observations on the effectiveness of a yeast-peanut butter mixture in vitamin B complex deficiencies. *South. M. J.* **34**:159-161, 1941.
31. Aballi, A. J., and Escobar Aces, A. Trastornos digestivos por carencias de factores del complejo vitaminico B. *Bol. Soc. cubana de pediat.* **12**:91-135, 1940.
32. Sydenstricker, V. P. Syndrome of multiple vitamin deficiency. *Ann. Int. Med.* **15**:45-51, 1941.
33. Bercovitz, Z. Recent advances in the treatment of chronic ulcerative colitis. *M. Clin. North America* **24**:683-704, 1940.
34. Ludden, J. B., Flexner, J., and Wright, I. S. Studies on ascorbic acid deficiency in gastric diseases: incidence, diagnosis and treatment. *Am. J. Digest. Dis.* **8**:249-252, 1941.
35. Field, H., Jr., Robinson, W. D., and Melnick, D. Vitamins in peptic ulcer. *Ann. Int. Med.* **14**:588-592, 1940.
36. Ingalls, T. H., and Warren, H. A. Asymptomatic scurvy: its relation to wound healing and its incidence in patients with peptic ulcer. *New Eng. J. Med.* **217**:443-446, 1937.
37. Minnich, V., Wright, S. T., Moore, C. V., and Spies, T. D. Whole blood and plasma ascorbic acid concentrations in patients with pellagra and associated deficiency diseases. *Proc. Soc. Exper. Biol. & Med.* **45**:441-446, 1940.
38. Irvin, J. L., Kopala, J., and Johnston, C. G. The absorption of carotene from isolated intestinal loops. *Am. J. Physiol.* **132**:202-210, 1941.
39. May, C. D., and McCreary, J. F. The absorption of vitamin A in celiac disease: interpretation of the vitamin A absorption test. *J. Pediat.* **18**:200-209, 1941.
40. Ralli, E. P., Bauman, E., and Roberts, L. B. The plasma levels of vitamin A after the ingestion of standard doses: studies in normal subjects and patients with cirrhosis of the liver. *J. Clin. Investigation* **20**:709-713, 1941.
41. Dyer, H. M., and Roe, J. H. The relation of nutrition to gastric function. IV. The effect of vitamin A deficiency. *Am. J. Digest. Dis.* **8**:333-337, 1941.
42. Herrin, R. C. Gastric emptying time and acidity in avitaminosis A in dogs. *Am. J. Digest. Dis.* **7**:164-166, 1940.
43. Földes, F., and Vajda, G. Effect of vitamin A on the secretion of gastric juice in deficient hydrochloric acid production. *Brit. M. J.* **1**:317, 1941.
44. Seelig, S. F. Treatment of gastric ulcer with vitamin A. *Guy's Hosp. Rep.* **90**:41-54, 1941.
45. Fridericia, L. S., Gudjonsson, S., Vimtrup, B., Clemmesen, S., and Clemmesen, J. Stomach lesions in rats kept on diets deficient in vitamin A. *Am. J. Cancer* **39**:61-69, 1940.
46. Beck, S., and Peacock, P. R. Gastro-papillomatosis due to vitamin A deficiency induced by heated fats. *Brit. M. J.* **2**:81-83, 1941.
47. Stryker, W. A., and Janota, M. Vitamin A deficiency and intestinal permeability to bacteria and toxin. *J. Infect. Dis.* **69**:243-247, 1941.
48. Abels, J. C., Gorham, A. T., Pack, G. T., and Rhoads, C. P. Metabolic studies in patients with cancer of the gastro-intestinal tract. I. Plasma vitamin A levels in patients with malignant neoplastic disease, particularly of the gastro-intestinal tract. *J. Clin. Investigation* **20**:749-764, 1941.
49. Albright, F., and Stewart, J. D. Hypovitaminosis of all fat-soluble vitamins due to steatorrhea. *New Eng. J. Med.* **223**:239-241, 1940.
50. Warner, E. D., Spies, T. D., and Owen, C. A. Hypoprothrombinemia and vitamin K in nutritional deficiency states. *South. M. J.* **34**:161-163, 1941.

CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

ANTE-MORTEM AND POST-MORTEM RECORDS AS USED IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

CASE 28141

PRESENTATION OF CASE

First admission. A thirty-five-year-old Russian butcher's helper was admitted to the hospital because of pain and disability in the right elbow for one month.

A year before entry, the right elbow was slammed by the door of an auto in which the patient was riding. There was considerable local pain at the time, but no swelling, discoloration or actual disability was noted. Since then, he had experienced occasional slight pain along the inner aspect of the elbow. In the month before entry, the pain tended to become severer, and he was unable to straighten the elbow fully. There were no constitutional symptoms.

On admission, the patient appeared thin and pallid. There was a smooth, rounded swelling over the internal condyle of the right humerus, enlarging this landmark to about twice its normal size. The skin overlying this mass was not attached, or otherwise altered. The mass was tender posteriorly only (in the region of the ulnar nerve). Extension was limited by about 20°, but other movements were normal. There was no evidence of interference with the ulnar nerve. The other extremities were normal, and the rest of the physical examination was negative.

The temperature, pulse, respirations and blood pressure were normal.

Examination of the blood showed a red-cell count of 4,800,000, and a white-cell count of 10,500 with 72 per cent polymorphonuclears. The blood calcium was 11.0 mg. and the phosphorus was 3.3 mg. per 100 cc.; the phosphatase was 3.4 Bodansky units. The blood Hinton reaction was negative. The total cholesterol was 114 mg. per 100 cc.

A roentgenogram showed a mutilocular cystic area in the medial condyle of the right humerus. The bone appeared thickened anteriorly, without interruption of the cortex. The upper aspect of the facet of the trochlea seemed involved; this prevented complete extension of the elbow. The bone surrounding the lesion showed normal structure.

A roentgenogram of the left elbow was negative.

On the third hospital day, the medial aspect of the lower end of the right humerus was exposed and incised; this revealed a cavity from which portions of soft, friable yellowish tissue and of soft, pinkish currant-jelly-like tissue were readily curetted. The cavity was thoroughly curetted, not packed with bone chips, and closed by approximation of the muscle layers. Microscopic examination of the material removed showed a benign giant-cell tumor. The patient was discharged on the sixth postoperative day.

Second admission (two and a half years later). The patient was followed in the Tumor Clinic, receiving three courses of roentgen-ray therapy, of 800 r each. There was a gradual increase of flexion deformity to about 65°. The patient, however, was able to work as a mechanic, not lifting much weight. He was readmitted to the hospital because there was some question of increase in size of the residual mass in the elbow.

On re-examination, the general physical condition was normal. The left elbow was held in 65° flexion. Extension was limited to 70°, and flexion was limited to 120°. Full and painless pronation and supination were possible. There was a circumscribed, bony hard swelling over the medial humeral epicondyle, which was firmly attached to the bone and tender in some areas. There was full ulnar-nerve function. The axillary lymph nodes were not enlarged.

The temperature, pulse, respirations and blood pressure were normal.

Examination of the blood and urine was essentially as before. The blood calcium was 10.6 mg. and the phosphorus 3.2 mg. per 100 cc.; the phosphatase was 2.9 Bodansky units.

A roentgenogram of the chest showed some emphysema and pulmonary fibrosis, but no metastatic lesions. A roentgenogram of the right elbow showed no definite increase in the size of the lesion.

On the tenth hospital day, an operation was performed.

DIFFERENTIAL DIAGNOSIS

DR. CHANNING C. SIMMONS: This man had some bone condition of the lower end of the humerus. There are many things to be considered, but roughly these bone conditions can be divided into five categories: unusual conditions, such as a coccidioidal infection and an echinococcal cyst, which I have never seen, although they occur in other parts of the country; an ordinary inflammatory lesion, such as tuberculosis, syphilis or osteomyelitis; metabolic disease, parathyroid disease or primary disease of bone, such as Paget's disease; metastatic tumors; and primary bone tumors, either malignant or benign.

The first category, the unusual bone conditions, can probably be excluded, although at one time I made a list of forty-five different conditions that I have seen erroneously diagnosed as osteogenic sarcoma. The inflammatory conditions — tuberculosis, syphilis and osteomyelitis — must be considered. The joint was not involved. There was no evidence of tuberculosis elsewhere. The blood Hinton reaction was negative. Osteomyelitis is not suggested by either the physical examination or the laboratory findings. Metabolic disease may be well ruled out, for the blood chemical findings were normal, and there was no evidence of any disease of the other bones. The general physical examination was not remarkable, except that the patient was a rather slender man.

So far as metastatic tumors are concerned, there is no evidence of any tumor as a primary source of metastases. This condition had existed for three and a half years since the onset. The duration was one and a half years at the first admission, and the second admission was two and a half years later.

That brings us down to a primary tumor, either benign or malignant. A history of trauma is obtained in about 40 per cent of the cases of primary bone tumors. I think it is fairly safe to say that the tumor in this case was not malignant, for a malignant bone tumor would give some evidence of remote metastases three and a half years after onset. Giant-cell tumors often appear after injury in the humerus and in the knee. In the femur, they are apt to arise in the inner condyle; in the humerus, in the outer condyle. They originate in the medulla, cause bone destruction, extend to the cartilage, as this one did, without breaking through into the joint, and form an expanding bone tumor.

This x-ray film, I take it, is an early one. The outline of the periosteum is unbroken except at one point. There is some expansion in this other film. The gross description of the tumor removed at the first operation is certainly compatible with that of a giant-cell tumor.

These tumors appear in two forms: a currant-jelly-like, very vascular tissue, and fibrous tissue that is yellow in color, probably owing to deposits of hemosiderin and lipoid material. Following the first operation, the patient received x-ray treatment with no appreciable improvement, and he re-entered with essentially the same condition — a little more advanced. The second x-ray film shows bulging of the internal condyle down to the joint surface. I think that the limitation of motion was partly due to mechanical interference.

My diagnosis in this case is giant-cell tumor. Such tumors are cured at times by excision or curetting, at times by radiation; in a study of a large series, about 30 per cent of the patients were not cured by either method and came eventually to amputation. About 7 per cent undergo malignant change. As I have seen these cases, the defect never fills up with normal bone, and if bone chips are placed in the cavity after curetting they are absorbed. My diagnosis is giant-cell tumor, running the course that many of them do.

DR. TRACY B. MALLORY: You would not be seriously worried over the possibility of malignant tumor?

DR. SIMMONS: No; I should not.

CLINICAL DIAGNOSIS

Giant-cell tumor, right elbow.

DR. SIMMONS'S DIAGNOSIS

Giant-cell tumor of humerus.

ANATOMICAL DIAGNOSIS

Giant-cell tumor of humerus.

PATHOLOGICAL DISCUSSION

DR. MALLORY: This lesion was once again curetted, and the gross material on this occasion was rather fibrous, with many yellow spots in it. It did not show any of the currant-jelly appearance. On microscopic examination, there are areas of quite characteristic giant-cell tumor. These are interspersed with areas of rather dense fibrosis in which a good many cholesterin-filled foam cells are found. There are a few trabeculae and osteoid material, but nothing that suggests malignant lesions. I suspect that the unusual degree of fibrosis could perhaps be attributed to the x-ray treatment that the patient had received off and on during this period.

DR. SIMMONS: I think that is the usual story — increase in fibrosis following either curettage or x-ray treatment. The cavity never fills in with normal bone.

DR. GEORGE W. HOLMES: I should like to know, although I was present at the time this question of operation was discussed, just why they operated. I presume that it was to improve function, and I wonder if operation would improve function, because there is nothing in the lesion as I see it in the x-ray film to make me think of a malignant tumor; as a matter of fact, it really did improve somewhat under radiation. The outlines are sharp, it has not grown any in two years, and although it has not filled in with new bone, it is at least quiescent.

DR. MALLORY: The patient, who was a manual worker, had considerable limitation of function and found it difficult to work.

DR. GEORGE W. VAN GORDER: After considerable discussion in the Tumor Clinic and in the Orthopedic Staff, it was decided that the wisest operative procedure to carry out on this patient's arm was excision of the tumor, in addition to an arthrodesis of the elbow joint, allowing the radial head to remain free to rotate in a normal way on the remaining external condyle of the humerus.

The reason that a movable elbow joint was not considered advisable was that the tumor occupied too great a portion of the articular surface to allow for normal motion or stability after its excision. In other words, more than half the articular surface of the lower end of the humerus would have had to be sacrificed, and this would have resulted in a useless joint. An alternative was to perform a complete excision of the lower end of the humerus, but this would also have involved too great a portion of bone to permit any future stability or strength in the joint. Since this patient is the father of a family and has to work, and since he could not do his work with a flail elbow, it was decided that a firm ankylosed joint in an optimal position of election would be the most satisfactory answer to his problem from an economic and social point of view. The patient was asked about the type of work that he performed and the angle at which his elbow was most useful in carrying on his job, the idea being that if the joint were solidly fused at the proper angle, it would later be of the greatest service to him. These matters were all considered before the operative procedure was carried out.

In the surgical procedure itself, the tumor was completely excised, and following excision, the cartilaginous surface of the ulna and its adjacent humeral articular surface were removed, after which a long vitallium bone plate, which had previously been bent at the proper angle, was applied to the posterior aspect of the joint, with three screws to hold it to the lower end of the humerus and with three screws to the shaft of the ulna.

Following application of this plate, the elbow joint seemed to be firm and in its proper position, and the upper end of the radius was not interfered with at all, so that full rotation of the forearm remained undisturbed. Two drill holes, each 6 mm. in diameter, were then made through the external condyle of the humerus across the joint line into the ulna, and into these drill holes two tibial bone grafts were driven, which acted as dowels, anchoring the two bones together. A third bone graft was placed between the humerus and ulna in another direction, avoiding the radiohumeral articulation.

The wound was then closed, in the hope that solid union would take place between the ulna and external condyle of the humerus and that rotation motion would be preserved for the forearm. Should this result be obtained, the patient will be able to continue his job or at least do heavy work with a very useful arm.

CASE 28142

PRESENTATION OF CASE

A thirty-year-old housewife was admitted to the hospital because of a mass in the upper jaw.

The patient was well until six months before entry, when, in the fifth month of an otherwise normal fifth pregnancy, she noted a slightly painful gray, purulent swelling on the upper jaw, where a tooth had been extracted several years previously. Two weeks later, a smooth, firm, slightly painful lump appeared at the same site on the buccal side of the jaw. It grew rapidly for a month, and then it was excised in another hospital. Following this, there was a recurrence of the lesion, with spread over a larger area of the jaw. The mass was re-excised in the other hospital on two subsequent occasions. The pathological diagnosis each time was epulis. Following the last excision, two months before entry, the mass became so large that the patient had trouble in closing her mouth, and in chewing her food. At times, there was a dull ache in the jaw, with occasional radiation to the neck. There was no pain elsewhere. The pregnancy terminated in normal delivery two weeks before entry.

The past history was noncontributory. Four earlier pregnancies had resulted in two miscarriages and two living children. The family history was irrelevant.

On admission, the patient appeared well developed and nourished. The left cheek was distended by a firm mass, extending from the midline near the nose back to within 2 cm. of the ear, and from below the eye down to the mandible. The left nostril was not obstructed. Just under the lip, the lower edge of the mass was denuded of epithelium, appearing yellow brown with spots of old blood. Within the mouth, the swelling approached the midline of the hard palate, irregularly. The buccal aspect of the left maxilla was occupied entirely by the mass. The swelling was moderately tender. Both tonsils were enlarged, and an apparent lymph node was palpable, in the left supraclavicular region. The spleen was questionably palpable, and there was moderate suprapubic tenderness. Pelvic examination showed normal puerperal changes. General physical examination was otherwise negative.

The blood pressure, temperature, pulse and respirations were essentially normal.

Examination of the blood and urine was essentially negative. The blood calcium was 10.4 mg.

and the phosphorus 3.4 mg. per 100 cc., and the phosphatase was 3.5 Bodansky units.

Roentgenograms of the jaw showed an area of destruction in the left maxilla extending from the spinous process and the midline back to within 0.5 cm. of the posterior margin. The involved bone appeared moth-eaten and almost completely destroyed. The apexes of the bicuspids, cuspids and lateral incisor were involved. A large soft-tissue mass extended beneath the lip and cheek, including several fine bone spicules. There was an apparent bulge into the left maxillary antrum. This cavity was enlarged in all directions, and its wall appeared broken through in several places. A roentgenogram of the chest was negative.

A biopsy of the mass was taken on the second hospital day, and a week later an operation was performed.

Differential Diagnosis

Dr. Harold G. Tobey: This is a rather short history of what apparently was a malignant tumor. We can probably rule out acute or chronic infection of the sinuses. The entire history was too short for any chronic infection, except possibly an osteomyelitis, which might develop as quickly as this, but probably would not. The only specific infection we must consider is the possibility brought up by the yellow-brown spots, particularly the yellow, which might suggest actinomycosis. There is no bacteriologic report; presumably, that was thought of and ruled out. Here again, six months is a rather short time for such a rapid spread, even of actinomycosis. So that we are brought down to the possibility of a malignant growth.

The alveolar process and the sinuses are subject to the usual malignant growths, carcinoma and sarcoma, and at times some of the lymphomas. It is significant that a few years previously a tooth had been extracted, and the tumor presumably occurred at the site of this tooth. The tumor was removed, and a diagnosis of epulis was made. It is possible that the diagnosis was incorrect. The ordinary epulis presents a picture similar to that of a benign giant-cell tumor of bone, but sarcomatous "degeneration" of the latter is conceivable. The recurrence happened in exactly the same place where the mass had been removed. So far as epithelioma is concerned, it is usually much more slowly progressing. It may start inside the antrum, possibly where the tooth was extracted. The fact that both tonsils were enlarged makes me think of the possibility of lymphoma, but there was practically no adenopathy. One lymph node was palpated in the left supraclavicular region, but nothing is said about palpation of lymph nodes elsewhere.

May we see the x-ray films?

Dr. George W. Holmes: These two small films show the extent and character of the lesion better than any of the others. It is quite large, moderately dense, and, what is most important, shows spicules of bone within the tumor substance. It has partially destroyed the antrum, and there is bulging of the bone, which is a little unusual. A rapidly growing malignant tumor does not as a rule cause bulging, but simply destroys the walls. This has done both. It is essential to know whether the floor of the orbit is destroyed or not. We thought it was at least infiltrated by this growth and partially destroyed. This tumor has some of the characteristics of benign tumor and some of the characteristics of a malignant tumor. I think it would be fair to say that it would be very difficult to explain the infiltration of bone and the presence of spicules in a benign lesion.

Dr. Tobey: The benign lesions usually expand the bone, and the bone is absorbed by pressure.

There is a tumor called a "pregnancy tumor," which I have never seen and know nothing about, but it does occur about the alveolar processes.

There are other conditions that might be considered; one of them is mucocele of the sinus, which is more common in the frontal sinus, with destruction of the bone and smooth surfaces, but this is altogether too rapidly growing for a mucocele. In the absence of any acute infection and in view of the involvement and active destruction of the bone, I should say that this tumor was probably an osteogenic sarcoma.

Dr. Channing C. Simmons: I saw this woman, and the question of whether this was a pregnancy tumor arose. I reviewed two articles on the subject, and the largest pregnancy tumor reported was 1.5 cm. in diameter. I also talked with some of the dental surgeons about pregnancy tumors of the mouth, and was told that a shaggy appearance of the mucous membrane over the alveolar process was not uncommon. This tissue is very vascular, but it usually disappears after delivery. I have also seen angiomas about the mouth and elsewhere that increased in size during pregnancy and went down afterward. There is apparently some metabolic disturbance that makes them grow. This particular tumor was a new growth of either sarcomatous or possibly adamantinomatous type; but it was very rapidly growing for the latter. The other thing I might say is that a tumor with a histologic picture such as this, if it occurred in the long bone, would probably cause death with metastasis, but in the jaw such tumors do not often metastasize.

A Physician: What about ossifying fibromas?

Dr. Simmons: I have never seen one. I have

seen diffuse fibromas of the upper jaw, where the antrum is thickened and the whole upper jaw transformed into rather soft ossifying tissue. They apparently arise from the inner process of the superior maxilla and fill the antrum.

DR. HOLMES: They cause a much denser shadow than this one did, and completely obliterate the entire area of the sinus.

DR. SIMMONS: They are slowly growing tumors and occur in patients of about ten to fifteen years of age.

DR. LANGDON PARSONS: The last biopsy taken from the tumor itself was reported as ossifying fibroma. When the entire maxilla was removed and the specimen in the pathologist's hand, the report was still ossifying fibroma. So far as the orbital floor was concerned, it was completely destroyed. This tumor had definitely grown under observation in the week that the patient spent on the wards.

DR. SIMMONS: Was it encapsulated?

DR. PARSONS: Yes, except for the part that had broken into the orbit.

DR. TOBEY: Is that not quite fast for sarcoma? It suggests a rapidly growing lymphoma.

DR. SIMMONS: Do you think that the pregnancy had anything to do with the rapidity of growth?

DR. TRACY B. MALLORY: I do not know the answer to that. One suspects it, of course. Pregnancy can influence the growth of a variety of tumors.

CLINICAL DIAGNOSIS

Ossifying fibroma of maxilla.

DR. TOBEY'S DIAGNOSIS

Osteogenic sarcoma of maxilla.

ANATOMICAL DIAGNOSIS

Osteogenic sarcoma of maxilla.

PATHOLOGICAL DISCUSSION

DR. MALLORY: The early biopsies on this tumor were all rather inadequate, and for that reason the diagnosis was not made sooner. The final specimen showed undifferentiated, anaplastic cells embedded in osteoid tissue, and on a histologic basis one could not call it anything but an osteogenic sarcoma.

What the outlook is I do not know. As Dr. Simmons said, tumors in this area often behave more benignly than their histologic characteristics lead one to predict, so that it is possible that the patient has been cured and will not have a metastasis. Had this tumor occurred in a long bone, I should not hold out any hope whatever.

DR. HOLMES: Did the patient have any radiation?

DR. PARSONS: She had had some before she came here. We were never able to find out how much.

DR. MALLORY: The immediate results of operation were excellent. It was possible to excise all the visible tumor, and in spite of the fact that there is no floor to the orbit, the eye is not sagging and the vision is good.

The New England
Journal of Medicine

Formerly

The Boston Medical and Surgical Journal

Established in 1828

Owned by the Massachusetts Medical Society and Published under the Jurisdiction of the Committee on Publications

Official Organ of
The Massachusetts Medical Society
and
The New Hampshire Medical Society

Editorial Board

Joseph Garland, M.D.
William B. Breed, M.D.
George R. Minot, M.D.
Frank H. Lahey, M.D.
Shields Warren, M.D.
George L. Tobey, Jr., M.D.
C. Guy Lane, M.D.
William A. Rogers, M.D.
Stephen Rushmore, M.D.
Henry R. Viets, M.D.
Robert M. Green, M.D.
Charles C. Lund, M.D.
John F. Fulton, M.D.
A. Warren Stearns, M.D.
Dwight O'Hara, M.D.
Chester S. Keefer, M.D.

Associate Editors

Thomas H. Lanman, M.D.
Henry Jackson, Jr., M.D.
Donald Munro, M.D.

Walter P. Bowers, M.D., Editor Emeritus
Robert N. Nye, M.D., Managing Editor
Clara D. Davies, Assistant Editor

Subscription Terms: $6.00 per year in advance, postage paid, for the United States (medical students, $3.50 per year); Canada, $7.04 per year, Boston funds; $8.52 per year for all foreign countries belonging to the Postal Union.

Material for early publication should be received not later than noon on Friday.

The Journal does not hold itself responsible for statements made by any contributor.

Communications should be addressed to the *New England Journal of Medicine*, 8 Fenway, Boston, Massachusetts.

EARLY RISING AFTER OPERATIONS

The supposed necessity of keeping patients in bed for a more or less arbitrary minimum period of about a week and in the hospital for ten days after many of the less severe major operations not associated with prostrating illness has recently been questioned in several countries.[1-4] Leithauser and Bergo's[1] study of this subject presents data on 370 cases subjected to appendectomy and on 66 cases having had other operations. The study appears to prove that nothing harmful is likely to happen to these patients if they get out of bed on the day after operation. The authors even claim that this method of postoperative care gives excellent results, since there was not a single case with pulmonary complications, dehiscence, postoperative hernia, thrombophlebitis or death. Their treatment really consists of a logical extension of certain ideas concerning the prevention of pulmonary complications that have recently been enthusiastically adopted by certain surgeons, although first proved valuable twenty-five years ago.[5] The late Dr. E. Amory Codman, of Boston, once expressed the opinion that the time would come "when interval and prophylactic appendectomy would be performed through a McBurney incision under local procaine anesthesia in the surgeon's office, and the patient would be allowed to go home a few hours later."[6]

The details of Leithauser and Bergo's[1] treatment are as follows:

> After operation the patients were turned frequently in bed and were instructed to be active and to take deep breathing exercises at regular intervals. On the first postoperative day, provided conditions were satisfactory, they were assisted in sitting on the edge of the bed [after assuming the right lateral position] and then in standing beside the bed for deep breathing exercises. [This consumed only a few moments.] While in each position they were instructed to take several deep inhalations and were urged to cough. This procedure seldom failed promptly to clear the lungs of accumulations of mucus. After this was accomplished they were permitted to walk about the room and to sit in a chair for a few moments, and then they returned to bed. On returning they sat on the edge of the bed and reclined on the right shoulder. These sitting-up and ambulatory exercises were always first carried out under the supervision of one of us. Such exercises were then repeated during the first postoperative day with the assistance of a nurse, and thereafter the patients were encouraged to increase their activities voluntarily. They left the hospital by automobile. . . .

It is unfortunate that no statement is made regarding the time of determination of the presence or absence of postoperative hernia, since many surgeons are skeptical of such findings unless systematic search has been made at least six months after operation. It goes without saying that the authors' method of suturing wounds, in which No. 0 chromic catgut and steel wire or nylon were employed, was eminently satisfactory.

The average duration of confinement to bed of the appendectomy patients was 1.5 days: 75 per

cent of them arose on the first day, 12 per cent on the second, and 8 per cent on the third. The average stay in the hospital was 2.3 days: 37 per cent of the patients left on the first day, 32 per cent on the second, 14 per cent on the third, and 10 per cent on the fourth. These figures are extremely interesting and significant, and bear comparison with those of similar cases treated according to more orthodox methods. For example, in the months of March and September, 1941, of 39 ward and 267 semiprivate patients who held policies issued by the Massachusetts Hospital Service (Blue Cross) and who were operated on for appendicitis (all types), the total stay in the hospital averaged 10.6 and 12.5 days, respectively.[7] Furthermore, according to the statements of six prominent Boston surgeons,[8] the average time for the earliest getting-up of their private and ward patients with simple appendectomies is 5.7 days, with an average time of 6.7 days for all cases, and the average time for the earliest discharge from the hospital is 8.3 days, with a slightly higher average for all cases.

From these data, it is evident that an appreciable difference exists between the times of the cases treated by Leithauser and Bergo and those given the usual postoperative care. One might argue that patients should be allowed to get up one or two days earlier without further ado, thereby saving that much time in the hospital. Many believe, however, that such a procedure might not be so safe as really early rising, because it is likely that most wounds are stronger on the first and second days after operation than they are for the following week, owing to the well-known "lag period" in healing and the gradual weakening of certain suture material. In any event, it is possible that great savings in complications, let alone costs, would arise following the general adoption of the early-rising technic. It would be well worth while for others to experiment along this line.

References

1. Leithauser, D. J., and Bergo, H. L. Early rising and ambulatory activity after operation: means of preventing complications. *Arch. Surg.* 42:1086-1093, 1941.
2. Mermingas, K. Die Appendektomie ohne folgende Muskelnaht. *Zentralbl. f. Chir.* 60:553, 1933.
3. Mukhina, M. V. Early rising after appendectomy in acute period. *Vestnick khir.* 40:231-235, 1935.
4. Khromov, B. M. Value of early rising after operation in prevention of postoperative pulmonary complications. *Sovet. khir.* 9:389-397, 1936.
5. Pool, E. H. Systematic exercises in postoperative treatment. *J. A. M. A.* 60:1202-1204, 1913.
6. Stewart, J. D. Surgical care and operative technic. *New Eng. J. Med.* 225:620-625, 1941.
7. Cahalane, R. F. Personal communication.
8. Personal communications.

THE CONTROL OF CANCER

In times when practically the total effort of this country is aimed toward a destruction of the young and healthy men of other countries, it seems almost useless to attempt to maintain interest in cancer control. However, regardless of war and sudden death, cancer will continue to make its inroads, sometimes taking the most useful and productive minds from the community. Because of the character of the disease itself and its high rate of mortality, there are few maladies that can compete with it from the standpoint of economic loss. Hence, even in these days, the medical profession, with its continuous contacts with the victims of cancer, should keep in mind the menace of this disease and the value of its control. In addition to their heavy emergency obligations, physicians must not forget this ever-present threat to life and happiness. Of special importance are the detection and cure of early cases of cancer, to lessen the burden on the hospital facilities of the community that is made all too heavy by the advanced or terminal cases of the disease.

In the past, notable gains in cancer control have been made in Massachusetts, and the American Society for the Control of Cancer is doing much throughout the country to check the advancing mortality from this disease. Ignorance, fear and procrastination should not be permitted to turn curable cases of cancer into hopeless ones.

For the past few years, April has been designated as "Cancer Month" by proclamation of the President. In the pressure of world events, this designation seems about as futile as a last year's newspaper, but just as the lesson to be learned from last year's newspaper was there for all to see, the knowledge of what should be done to control cancer is almost as plainly written, and fully as easily forgotten.

MEDICAL EPONYM

Neisser's Diplococcus

Albert Neisser (1855–1916), when he was an assistant in the dermatologic clinic at the University of Breslau, published his paper "Über eine der Gonorrhoe eigenthümliche Micrococcusform [A Form of Micrococcus Peculiar to Gonorrhea]" in the *Centralblatt für die medicinischen Wissenschaften* (17: 497–500, 1879). A portion of the translation follows:

> If gonorrheal pus is spread as thinly as possible on a glass slide after Koch's method, allowed to dry and stained by simply flooding with an aqueous solution of methyl violet, and dried again, examination of the preparation under high power with the light cut down as little as possible will show at first glance, in addition to the dark violet-blue and variously shaped nuclei of the pus cells (the protoplasm of which is also stained, but only faintly), a number of more or less abundant clumps of micrococci. These have a quite characteristic and promptly recognizable typical form. . . . Nearly always two micrococci are seen lying close together—so closely that they give the impression of a single organism which is roll-shaped or biscuit-shaped, resembling a figure eight.

R. W. B.

MASSACHUSETTS MEDICAL SOCIETY

COMMITTEE ON MATERNAL WELFARE

Case History: Curettage causing perforation of the uterus and fatal sepsis

Because of continued bleeding, a thirty-year-old primipara entered the hospital twenty-five days after the delivery of a stillborn baby. The past history was irrelevant. There was no evidence of previous illness. The heart, lungs and blood pressure were said to have been normal. There is no record of a blood examination at the time of admission, and no description of the patient's labor. On admission, a curettage was performed, and in the process the uterus was perforated at the junction of the internal os and the anterior wall. According to the record, no intestine was brought down or injured. As soon as it was appreciated that the uterus had been perforated, the operation was stopped, and a gauze strip was placed in the perforation. The patient ran a septic course for three weeks. At the end of this time, the temperature reached normal and remained so for a week, when transfusion was performed. There is no evidence in the record of the blood picture that justified this transfusion. The transfusion itself was followed by a slight febrile reaction but the patient was sent home the following day. She remained in bed at home for a week, re-entered the hospital, and died of fulminating septicemia in less than twenty-four hours.

Comment. It is unfortunate that the record does not give more specific details of the delivery and subsequent convalescence. It is quite possible that the continued bleeding was caused by some small piece of placenta, which may have been adherent and may have had to be removed manually at the time of delivery. It is probable that this patient had fever before she entered the hospital; in that event, invasion of the uterus, unless the hemorrhage was profuse, was contraindicated. The fever, which is reported to have followed the curettage, in all probability meant that the uterus was harboring a low-grade infection at the time of entry and that the operative procedure of curettage broke down Nature's defensive wall and resulted in a spread of infection that demonstrated itself in the fever, which lasted for three weeks. It is quite probable that the perforation of the uterus was an incident and had nothing to do with the final outcome. During the week that the patient was home in bed, the history does not tell whether or not the temperature was normal, but it probably was not. The transfusion must have been given because of a low red-cell count and possibly for the purpose of stimulating recovery from the anemia associated with infection. In itself, the transfusion could not have precipitated the ultimate septicemia.

This case illustrates primarily the seriousness of curetting any patient with a temperature following childbirth as well as, of course, following abortion. The uterus in such a case should be left absolutely alone except in the presence of frank hemorrhage, when intrauterine manipulation should be conducted in the gentlest fashion, preferably with the finger.

COMMITTEE TO REVISE THE BY-LAWS

The following is the revised copy of the by-laws of the Society that will be presented by the Committee to Revise the By-laws to the Council for approval at its special meeting on April 15.

J. Harper Blaisdell, *Chairman*
Carl Bearse, *Secretary*
John Fallon
Harold R. Kurth

* * *

CHAPTER I

Fellowship

Section 1. Applicants for fellowship in the Massachusetts Medical Society are required to satisfy the censors that they are not less than twenty-one years of age; that they are of sound mind and of good

character; that they have a Baccalaureate or Doctorate of Medicine from a medical school approved by the Council, or have received the approval of the Committee on Membership; that they have received a license to practice medicine within the United States or its territories; that they do not practice medicine in a manner contrary to the code of ethics of the Society; that they have made application according to the provisions of Chapter V; and that they have paid the examination fee of three dollars.

They shall appear personally before the censors and satisfy them that the above requirements are fulfilled.

Section 2. Applicants found to be so qualified shall, on paying the assessment for the current fiscal year (except as hereafter provided in Section 6 of this chapter) and subscribing to the by-laws and code of ethics, all within two weeks from the date of their examinations, be approved by the censors.

They furthermore shall, on confirmation by the president and by the secretary of the Society, be admitted fellows of the Society and shall receive certificates of fellowship in testimony thereof signed by the President and by the Secretary.

Section 3. Fellows having a legal residence in Massachusetts shall be known as "resident fellows"; all others, as "nonresident fellows."

Nonresident fellows shall receive the official publications of the Society and may attend Society meetings, but may not vote, hold office or receive protection under the medical defense act of the Society.

Section 4. Honorary fellowship may be conferred on distinguished members of the medical profession.

Associate fellowship may be conferred on eminent workers in the allied sciences.

Such fellowships may be conferred by a two-thirds vote of the Council at a stated meeting, provided written nominations therefor have been submitted by two or more fellows at a previous stated meeting and have been approved by the Committee on Membership.

Honorary and associate fellows may attend and address meetings of the Society, but shall not be accorded other rights or privileges, or be subject to assessment.

Section 5. Fellows who are sixty-five years of age or older whose assessments have been paid or remitted may, by vote of the Executive Committee, acting on recommendation of the Committee on Membership, become retired fellows.

They shall be in good standing, and may attend and address meetings of the Society, but shall not be accorded other rights or privileges, except that, on request annually, they shall receive the publications of the Society.

They shall not be subject to assessment.

Applications for retirement shall be addressed to the Executive Committee and sent to the Treasurer.

Retired fellows may, on their own request, be restored to active fellowship by the Executive Committee.

Section 6. Fellows shall be assessed such sums as are voted by the Council, and such additional sums as are voted by the district societies for their own use.

The fiscal year shall begin on the first day of January. Assessments shall be paid in advance. The first assessment paid by a fellow admitted to the Society following the December examinations shall cover his dues for the succeeding fiscal year and shall be the amount fixed for that year.

Assessments may be remitted by the Executive Committee on recommendation by the Committee on Membership.

Whenever a fellow owing more than one annual assessment pays in part, the payment or payments so made shall be considered as on the assessment or assessments longest due and for no others.

Section 7. Resignations shall be submitted in writing to the Treasurer, who shall deliver them to the Committee on Membership.

This committee shall submit them with recommendations to the Executive Committee for action.

Resignations shall be accepted only from fellows whose assessments have been remitted or paid in full.

Section 8. Fellows who, despite notification by registered letter from the Treasurer, have not paid assessments for two years, or who, despite notification by registered letter from a district treasurer, have not paid the assessments of their district society for two years, shall be deprived of the privileges of fellowship by the Executive Committee, acting on a report of the Committee on Membership, unless otherwise ordered.

Section 9. Fellows who have been convicted in a court of law of a crime involving moral turpitude or who have been guilty of attempts to harm the Society or to injure its usefulness; of advertising nostrums for sale or otherwise offering them to the public, or professing to cure disease by secret methods; of gross violations of these by-laws, of the code of ethics of the Society or of the American Medical Association; of presenting false certificates or false statements of character or of educational requirements; of accepting rebates on prescriptions or appliances; or of any other conduct unbecoming a physician, may be expelled from the Society or otherwise disciplined as provided in Chapter VIII, Section 9.

A fellow who has been deprived of his license to practice medicine in the Commonwealth shall automatically cease to be a fellow of the Society.

Section 10. Former fellows who desire to be readmitted following retirement, resignation not requested by the Committee on Ethics and Discipline, or deprivation of fellowship for arrears shall make application in writing addressed to the Executive Committee and sent to the Secretary.

Such applications shall be referred for investigation to the board of membership of the district society concerned, which shall report with recommendations to the Committee on Membership.

This committee shall report with recommendations to the Executive Committee.

The Executive Committee may readmit former fellows so recommended.

Section 11. Committees having under consideration the applications of former fellows (*a*) whose resignations have been requested by the Committee on Ethics and Discipline or (*b*) who have been

deprived of fellowship under the terms of Section 9 shall consult with the Committee on Ethics and Discipline before reporting their recommendations to the Council.

CHAPTER II

Meetings of the Society

Section 1. The annual meeting of the Society shall be held in Boston, on the second Wednesday of June, unless otherwise ordered by the Council.

The order of business shall be: (1) reading of the record of the last annual meeting; (2) report by the Secretary of changes in membership during the year; (3) report by the President on the state of the Society; (4) such other business as may lawfully come before the meeting; (5) annual oration.

Section 2. Special meetings of the Society may be called by the President, or by vote of the Council, and shall be called on written request by ten councilors or one hundred fellows.

Section 3. The deliberations of the Society shall be governed by parliamentary usage as interpreted by *Roberts' Rules of Order*, when not in conflict with the by-laws of the Society.

One hundred fellows shall constitute a quorum.

CHAPTER III

District Societies

Section 1. The boundaries of district societies may be changed, and new districts may be established, by the Council.

Section 2. The membership of each district society shall consist only of such fellows, whether active or retired, as have legal residences within the boundaries of the district, except in cases decided otherwise by vote of the Executive Committee.

Section 3. Any fellow wishing to transfer membership from one district society to another without a change of legal residence must so petition the Committee on Membership in writing, stating his reasons therefor.

The Committee on Membership shall report, after consultation with the officers of the two districts concerned, its recommendations to the Executive Committee for action.

Section 4. Each district society may adopt by-laws and regulations for the government of its own affairs and levy assessments, provided such by-laws and regulations are not in conflict with those of the Society.

Section 5. Each district society shall hold its annual meeting between the fifteenth day of April and the fifteenth day of May.

Each district society at this meeting shall elect by ballot from its active fellows: a president, who shall be *ex officio*, a vice-president of the Society; a vice-president; a secretary; a treasurer; councilors as below specified; four censors; a supervising censor; a commissioner of trial; a member of the Committee on Public Relations; a member of the Committee on Legislation; a member and alternate member of the Committee on Nominations.

Councilors shall be elected in number equal to one for every twenty active and retired fellows and a majority fraction thereof, as of the first day of January preceding.

Only councilors shall be eligible as supervising censors and members of the Committee on Public Relations and the Committee on Legislation.

Only councilors who have held this office for at least one year shall be eligible as members of and alternates to the Committee on Nominations. Members of and alternates to the Committee on Nominations shall not serve for more than five consecutive years and shall not be eligible for re-election for three years thereafter.

Only fellows who have been members of the Society for at least ten years shall be eligible as censors or supervising censors. The term of the supervising censors shall be five years. They shall not immediately succeed themselves. All supervising censors shall have been censors previously.

Councilors, censors, supervising censors, members of the Committee on Public Relations, members of the Committee on Legislation, members of the Committee on Nominations, and commissioners of trial shall take office at the close of the next annual meeting of the Society.

The councilors of each district society shall meet on call by the secretary at or as soon as possible after the annual meeting of the district society and elect two of their number to serve as member and alternate of the Executive Committee, in accordance with Chapter VII, Section 2.

Members of and alternates to the Executive Committee shall serve for three years and shall not be eligible for re-election for three years thereafter.

The term of office of the alternate shall be concurrent with the term for which the member was elected.

Vacancies that occur during the term of office of such member or alternate shall be filled promptly, by vote of the councilors of the district concerned, *ad interim*.

Section 6. The secretary of each district society, promptly after its annual meeting, shall report on appropriate forms, to the Secretary the names and residences of fellows elected, as provided in Chapter III, Section 5.

He shall promptly notify the Secretary, on the required form, of deaths of fellows in his district.

He shall also perform such duties as are defined in Chapter V.

He shall call, at or as soon as possible after the annual meeting of the district society and before the annual meeting of the Society, meetings of the district councilors to elect the member and alternate of the Executive Committee, and shall send to the Secretary the names of the member and alternate chosen.

He shall see that a new member or alternate is chosen in a similar manner to fill a vacancy as it occurs, as provided in Section 5.

Section 7. The treasurer of each district society shall collect the assessments of his district.

He shall furnish a list of fellows two years in arrears to the Committee on Membership for action as provided in Chapter I, Section 8.

CHAPTER IV

The Council

Section 1. The Council shall consist of councilors chosen by the district societies, the president, ex-presidents, president-elect, vice-president, vice-presidents *ex officiis*, secretary, treasurer, and assistant

treasurer of the Society, the secretaries of the district societies and the chairmen of all standing committees.

The Council each year shall hold three stated meetings in Boston, unless otherwise ordered by the Council. The annual meeting shall be held on the day next preceding the annual meeting of the Society. A stated meeting shall be held on the first Wednesday in October, and another, on the first Wednesday in February.

Special meetings may be called by the President, by vote of the Council, or by the written request of ten councilors.

Section 2. The deliberations of the Council shall be governed by parliamentary usage as contained in *Roberts' Rules of Order*, when not in conflict with the by-laws of the Society.

Fifty councilors shall constitute a quorum.

Section 3. The Council at its annual meeting, on nomination by the Committee on Nominations or from the floor, shall elect by ballot officers of the Society as follows: president-elect, who shall serve as president-elect until the second annual meeting of the Society after his election and shall, unless otherwise voted by the Council, become president on his installation in the course of that meeting, serving thereafter as president until the installation of his successor; a vice-president, secretary, treasurer, and assistant treasurer, all of whom shall assume the duties of office at the close of the annual meeting of the Society and shall hold office until their successors have been duly elected. Councilors only shall be eligible to the offices above-named.

The Council, in event of the death or the incapacity of the President-Elect, shall elect a president by ballot, at its next annual meeting, on nomination by the Committee on Nominations or from the floor.

The Council, at its annual meeting, on nomination by the Committee on Nominations or from the floor, shall elect by ballot a fellow to deliver an oration at the annual meeting of the Society the following year.

The Council at its annual meeting shall elect, on nomination by the President-Elect or from the floor, standing committees to serve for one year from the close of the annual meeting as follows: on Arrangements; on Publications; on Membership; on Ethics and Discipline; on Medical Education; on Public Health; on Medical Defense; on Society Headquarters; on Finance; and on Hospital Relations.

Section 4. The Council shall elect at the stated meeting in October, on nomination by the President or from the floor, the Auditing Committee, composed of two fellows who are not councilors.

This committee, following the close of the fiscal year, shall require by a certified public accountant an examination of the assets and securities of the Society in the custody of the Treasurer, and of the Treasurer's books and accounts.

This committee shall verify the accountant's examination and report its findings at the stated meeting of the Council in February.

Section 5. The Council may at any meeting fill vacancies in office or elect committees.

Section 6. The Council may vote to establish or abolish sections for the consideration of scientific papers at the annual meetings of the Society, and shall appoint the first chairman and secretary of a new section so established.

Each section shall elect annually a chairman and a secretary to serve for one year from the close of the annual meeting at which they are elected.

The duties of these officers shall be to arrange the programs of the meetings of their sections under the rules of the Council.

The chairman shall preside at the meetings of the section at the following annual meeting; the secretary shall take charge of the papers presented and shall transmit them promptly to the editor of the official journal of the Society.

Section 7. The Council shall, on nomination by the President or from the floor, elect delegates to the House of Delegates of the American Medical Association in accordance with the by-laws of that association.

It may, on nomination by the President or from the floor, elect delegates to such other medical meetings as it deems suitable.

Section 8. The Council shall vote the salaries of its officers and employees, the appropriations for its officers and committees, and such other appropriations as it deems suitable.

No officer or committee shall exceed the voted appropriation.

No salary to any officer or employee and no regular appropriation shall be increased except on recommendation of the Committee on Finance and by vote of the Council.

The Treasurer is authorized, on recommendation of the Committee on Finance, to pay such monies as may be necessary in the event of emergency, the existence of which shall be determined by the President.

CHAPTER V

Censors and Supervising Censors

Section 1. The supervising censors shall constitute a Board, which shall meet annually on the day appointed for the annual meeting of the Council. This board shall elect a chairman and also three of their members to sit with the Committee on Membership. Five supervising censors shall constitute a quorum.

The secretary of the Society shall act as secretary of the Board. He shall call special meetings at the request of the chairman or five supervising censors. He shall keep a permanent record of the proceedings of the Board, and shall provide materials necessary for conducting examinations of applicants for fellowship.

The Board at its annual meeting shall adopt a uniform plan for the examination of applicants.

The supervising censors, on request, shall be paid traveling expenses.

The supervising censors shall be chairmen of their respective boards of censors, and shall cause the examinations of applicants to be conducted in strict conformity to the plan adopted by the Board of Supervising Censors.

The censors of the several district societies shall meet for the examination of applicants semiannually on the first Thursday in May and on the first Thursday in December.

The approval of at least three censors shall be necessary to qualify an applicant.

An applicant failing two examinations may not again apply until three years have elapsed from the date of the last application.

Section 2. (*a*) The secretary of a district society may receive, *not later than* February 15 for the censors' examination in May or *later than* September 15 for the examination in December, an application for fellowship submitted on the proper form by an applicant whose legal residence is within the district of that society.

The secretary of the Suffolk District Society may receive, and officials of that society may act on, an application for nonresident fellowship.

The secretary of the district society shall verify each applicant's diploma and deliver his application to the Secretary *not later than* February 20 or September 20, respectively.

The official journal shall publish, in the first number on or after March 5 or October 5, a list of all applicants. This list shall include name, address, medical school and date of graduation of the applicant; name and address of the secretary of the district society concerned; and if a sponsor is required, the name and address of the sponsor.

Fellows are requested to send to the secretary of the district society concerned, *not later than*, respectively, March 20 or October 20, *confidential* written opinions on the qualifications of applicants.

(*b*) The secretary of a district society shall receive an application from a graduate of a discontinued medical school, a foreign medical school or any medical school not approved by the Council only when:

The applicant has possessed a license to practice medicine in the United States or its territories for at least five years;

The applicant has submitted with his application the name and address of a sponsor who is a fellow of the district society concerned; and

The sponsor has caused to be delivered by fellows of the Society to the secretary of the district society *confidential* written opinions on the qualifications of the applicant.

(*c*) The censors may admit to examination an applicant who is a graduate of a discontinued, foreign or unapproved medical school only when such applicant has been considered by the board of membership concerned and approved by the Committee on Membership.

The board of membership of a district society shall consist of the president, secretary and supervising censor.

It shall gather such information as it deems advisable to determine whether an applicant is conscientious, capable and reputable. It shall interview personally such applicant. It shall either approve or disapprove him for examination by the censors.

The secretary of the district society shall deliver to the chairman of the Committee on Membership, *not later than*, respectively, April 1 or November 1, all pertinent correspondence and other data together with the record of such applicant's approval or disapproval, with reasons therefor, by the board of membership.

The Committee on Membership shall have custody of such documents so long as needed and then shall deliver them to the custody of the Secretary; they shall remain *confidential*.

The Committee on Membership shall consider the application of each applicant approved for censors' examination by a board of membership. It shall determine finally whether or not such applicant may take that examination.

The Committee on Membership shall not consider the application of any applicant disapproved by a board of membership except on the written request of a majority of that board of membership.

Decisions on applications by the Committee on Membership shall be final, and shall remain in force for two years.

The Committee on Membership shall notify the secretary of the district society concerned and each applicant considered of its decision *not later than*, respectively, April 20 or November 20.

Section 3. The secretary of each district society shall be the secretary of the district board of censors.

He shall furnish applicants with forms adopted by the Board of Supervising Censors.

He shall keep a record of all applicants for fellowship, and see that each applicant pays the examination fee of three dollars, that this fee is sent *promptly* to the Treasurer, that each successful applicant subscribes to the by-laws and code of ethics and within two weeks pays the assessments for the current year.

He shall furnish each new fellow with a copy of the *Digest*, *By-laws*, *Code of Ethics*, and *Medical Defense Act* of the Society.

He shall present, on the proper form and promptly after each examination, a bill to the Treasurer for censors' services, together with a list of all applicants examined.

The secretary of each district society shall fill out, sign and deliver promptly to the Secretary certificates stating that the successful applicants have complied with the requirements of the by-laws.

Section 4. The censors and secretaries shall be paid from the funds of the Society three dollars for each applicant examined. The amount paid shall be divided equally among those officers attending and taking part in the examinations.

CHAPTER VI

Officers

Section 1. The President shall preside at the meetings of the Society, of the Council, of the Executive Committee and of the Committee on Public Relations.

He may call a meeting of any committee of the Society.

He shall approve all valid bills against the Society after they have been suitably endorsed by the officer, delegate, or chairman or majority of the committee that has incurred the indebtedness specified in the bill, as provided in Chapter VII, Section 1.

He shall sign the certificates of all delegates, and the diplomas of all new fellows if he is satisfied that they have met the requirements of Chapter I.

He shall nominate to the Council all members of committees, all delegates to other medical societies, all fellows to fill vacancies among the officers, councilors, censors and commissioners of trial of the Society, unless otherwise provided by the by-laws or by order of the Council.

He shall make appointments to fill vacancies *ad interim* in any of the offices of the Society.

He shall be a member *ex officio* of all committees.

He shall, in accordance with specific recommendations by the Committee on Ethics and Discipline, either admonish fellows or appoint a board of trial, as provided in Chapter VIII, Section 1.

He shall report on the state of the Society at the annual meeting.

He shall call one meeting of the Executive Committee between meetings of the Council, and others at his pleasure.

In the event of the death or incapacity of the President-Elect, the President, at the annual meeting of the Council, shall nominate members of standing and special committees, unless otherwise provided in the by-laws.

Section 2. In the absence of the President, the Vice-President shall perform the duties of the President; and in the absence of both, the senior *ex officio* Vice-President in point of membership in attendance shall perform the duties of the President.

Section 3. The President-Elect shall assist the President in the performance of his duties in such manner as the President may direct and in so doing shall be considered to represent the President.

At the annual meeting of the Council following the annual meeting at which he was elected, he shall nominate members of standing and special committees, unless otherwise provided for in the by-laws.

He shall be a member *ex officio* of all committees.

Section 4. The Secretary shall attend all meetings of the Society, the Council and the Executive Committee, and shall record their respective proceedings in separate volumes.

He shall cause to be engrossed and shall sign the diplomas of new fellows if satisfied that they have met the requirements of Chapter I, and shall issue all diplomas and certificates of fellowship.

He shall notify fellows of votes by the Council or Executive Committee granting permission to retire, to resign, to transfer district membership or to have dues remitted, and of votes depriving them of or reinstating them in the privileges of fellowship.

He shall be *ex officio* secretary of all boards of trial, the Board of Supervising Censors, the Committee on Publications and the Committee on Ethics and Discipline, and shall keep the records of each in separate volumes.

He shall have custody of the seal of the Society and of all books, papers, manuscripts, prints and paintings belonging to the Society, except such as are in charge of the Treasurer.

He shall issue notices of the meetings of the Council. He shall issue to every fellow one month before the annual meeting of the Society a program, listing the time and place of that meeting and of the stated meetings of the Council, the boards of censors for that year, and information concerning the payment of assessments and the distribution of publications; if there are any proposed amendments to the by-laws, he shall provide that each program is accompanied by a copy thereof.

He shall transfer fellows from one district to another under the terms of Chapter III, Section 3, and shall report to the Society at its annual meeting the changes in membership during the year.

He shall conduct official correspondence and shall notify officers, delegates and members of committees of their appointments and of their duties.

He shall keep a directory of the fellows, and shall publish the same, under the direction of the Committee on Publications, at such intervals as may be determined by the Council. He shall furnish this on request to fellows not in arrears.

He shall have jurisdiction over the work of the Executive Secretary.

He shall perform such other duties as the Society or the Council may require.

Section 5. The Treasurer shall collect and care for all monies due the Society and shall have custody of the treasury records. All monies received by any committee, officer or employee on behalf of the Society shall be paid forthwith to the Treasurer.

He shall be bonded in such sum and manner as may be directed by the Council, on recommendation of the Committee on Finance.

He shall, under the direction of the Council, sue for claims due the Society and shall sell, rent or lease any estate belonging to the Society.

He shall pay only such bills as have been countersigned by the proper officer or delegate, or the chairman or majority of the committee incurring the indebtedness, as provided in Chapter VII, Section 1, and have been approved by the President.

He shall render to the Council at its February meeting a full written report of the assets and liabilities on December 31 of the previous year, and also of the financial transactions of the Society during that year.

He shall attend the meetings of the Committee on Finance, furnish the committee with such data as it may require and shall make all investments and reinvestments of the Society's funds, with authority to buy or sell securities subject to the approval of this committee.

He shall arrange for the Cotting luncheons.

He shall familiarize the Assistant Treasurer with the fiscal concerns of the Society.

He shall perform such other duties as the Society or the Council may require.

Section 6. The Assistant Treasurer shall assist the Treasurer in the performance of such duties as the Treasurer may direct.

In event of the death or the incapacity of the Treasurer, the Assistant Treasurer shall assume the duties of the Treasurer until cessation of the incapacity or the next annual meeting of the Council.

He shall be bonded in such sum and manner as may be directed by the Council, on recommendation of the Committee on Finance.

Section 7. The Executive Secretary, under the jurisdiction of the Secretary, shall assist the officers, the Council and such committees as may request his services.

He shall hold office at the pleasure of the Executive Committee.

Section 8. The traveling and incidental expenses of the officers and committees elected by districts and of standing committees of the Society, on request, shall be paid by the Treasurer, on presentation of an itemized bill duly approved by the President.

CHAPTER VII

Committees

Section 1. Reports of committees containing recommendations that may require prolonged consideration shall be sent in abstract to the Secretary, at least six weeks before their presentation to the Council, for consideration by the Executive Committee and for publication in the official journal.

Every committee, annually on or before December 10, shall forward, to the chairman of the Committee on Finance, an estimate of its expenses for the ensuing fiscal year, which shall show the purpose of any proposed expenditure of $100 or more and a similar detailed statement of its expenditures for the current fiscal year to and including November 30 with an estimate of expenditures for the current month of December.

All bills $100 or more incurred by a committee shall be countersigned by a majority of said committee and forwarded to the President for his approval.

All bills less than $100 incurred by a committee shall be countersigned by the chairman of said committee and forwarded to the President for his approval.

Every committee shall render a written report to the Council at least once a year.

Committees Elected by the Districts

Section 2. The Executive Committee of the Council shall consist of the President, President-Elect, Vice-President, Secretary and Treasurer and a councilor from each district society, chosen as provided in Chapter III, Section 5.

The Executive Committee shall meet at the call of the President. It shall assist the President in preparing matters for consideration by the Council.

It shall act on all questions of retirement, resignation, remission of dues, deprivation of fellowship for arrears, reinstatement following deprivation of fellowship for arrears, and transfer of fellows from one district to another without change of legal residence.

The Executive Committee may appoint and dismiss the Executive Secretary.

It shall authorize or confirm action by the officers in emergency.

The Executive Committee shall perform such other duties as the Council may require.

Section 3. The Committee on Public Relations shall consist of the President as chairman and one councilor from each district society, elected as provided in Chapter III, Section 5.

It shall concern itself with the relations between fellows of the Society and the public.

Section 4. The Committee on Legislation shall consist of one fellow from each district society, elected as provided in Chapter III, Section 5.

It shall study, initiate and support measures to improve standards of medicine and promote the public welfare. It shall study and oppose such measures as it may deem contrary to the public welfare.

It may employ counsel, subject to approval of the President.

District legislative committees shall be auxiliary to and under the direction of this committee.

Section 5. The Committee on Nominations shall consist of one councilor, with another as alternate, from each district society, as provided in Chapter III, Section 5.

It shall nominate the officers and orator of the Society, and shall cause its report to be published in the notice of the annual meeting of the Council.

Standing Committees

Section 6. The Committee on Arrangements shall consist of five fellows.

It shall be responsible for all arrangements for the annual meeting of the Society.

The chairman shall furnish the Secretary, on or before April 15, with all the data necessary for the annual program.

The secretary of this committee shall record its proceedings in a volume which shall be filed with the Secretary.

Section 7. The Committee on Publications shall consist of five fellows.

It shall supervise the publications of the Society.

It shall publish, when ordered by the Council, a directory of the officers and fellows.

It shall appoint the Shattuck Lecturer in accordance with the provisions of the Shattuck bequest.

It shall inform all readers of papers and discussers of the following rules:

> All papers presented at the meetings of the Society shall be the property of the Society. No paper presented in the section meetings at the annual meeting shall occupy more than thirty minutes in its delivery. Each discussion shall be limited to five minutes, unless lengthened by vote of the meeting.
>
> All papers shall be ready for publication, typewritten and accompanied by suitable material for illustrations, if any, when read to the sections or to the Society; and as soon as read they shall be handed to the secretary of the section or of the Society for transmission to the editor of the official journal.
>
> Discussers shall correct and promptly return to the editor for publication, if deemed proper by this committee, the stenographer's transcribed notes of their remarks.

Section 8. The Committee on Membership shall consist of five fellows.

It shall consider applicants applying for fellowship according to the provisions of Chapter V, Section 2*c*.

It shall consider matters relating to honorary or associate fellowship, retirement, resignation, remission of dues, deprivation of fellowship for any cause, reinstatement following deprivation of fellowship for arrears, transfer of fellows from one district society to another, as provided for in Chapter III, Section 3, and shall make recommendations to the Council or the Executive Committee, as provided in Chapter I, Sections 10 and 11.

This committee shall confer with the representatives of the supervising censors as provided in Chapter V, Section 1.

Section 9. The Committee on Ethics and Discipline shall consist of five fellows.

It shall investigate and consider, either on charges submitted in writing or on its own initiative, any alleged or apparent offense on the part of any fellow, as provided in Chapter I, Section 9.

It shall either admonish him, request his resignation or report its findings to the President with its recommendations, if as a result of its investigations and after a hearing that has been requested by the fellow, the committee finds that he is guilty of such offense.

The President acting on such recommendations shall (*a*) censure the fellow, or (*b*) refer the matter to a board of trial, as provided in Chapter VIII, Section 1.

A member of the committee shall act as prosecuting officer in cases that come before a board of trial.

Section 10. The Committee on Medical Education shall consist of five fellows.

It shall consider matters relating to medical education.

It shall annually revise, subject to approval by the Council, the list of recognized medical schools and colleges.

Section 11. The Committee on Public Health shall consist of five fellows.

It shall foster the knowledge of the prevention and treatment of disease by any appropriate measures.

Section 12. The Committee on Medical Defense shall consist of five fellows.

It may appoint as auxiliary members one fellow in each district.

It shall act, under the provisions of the Medical Defense Act, on applications of resident fellows for legal services in the defense of suits for alleged malpractice.

It may take counsel with both plaintiff and defendant in threatened suits.

It shall report to the Committee on Ethics and Discipline any instance coming to its knowledge wherein a fellow, in connection with a suit for malpractice, has violated the code of ethics of the Society.

Section 13. The Committee on Society Headquarters shall consist of five fellows.

It shall supervise the maintenance of the Society Headquarters.

It shall acquire funds for expansion, subject to approval by the Council.

Section 14. The Committee on Finance shall consist of five fellows.

It shall recommend to the Council, at the February meeting, the budget for the current fiscal year.

The budget shall show in detail the proposed expenditures and their allocation to the various officers, employees, committees, or any other person or persons authorized to expend the same, and shall make available to any fellow on request the purpose of any proposed expenditure of $100 or more. The budget shall include for purposes of comparison similar items of expenditure for the previous year, if any.

It shall consider requests for extraordinary appropriations and shall refer them, with recommendations, to the Council for action.

It shall, at the close of the fiscal year after consultation with the Treasurer and with the approval of the Council, determine the amount to be refunded to the several district societies from the unexpended balance on December 31. This amount shall be apportioned among the district societies according to the number of annual assessments paid to the Treasurer before March 1.

Section 15. The Committee on Hospital Relations shall consist of five fellows.

It may appoint as auxiliary members one fellow in each district.

It shall concern itself with the relations between the fellows of the Society and hospitals.

CHAPTER VIII

Boards of Trial

Section 1. A board of trial shall consist of five of the commissioners of trial, appointed by the President, to consider charges against a fellow recommended for trial by the Committee on Ethics and Discipline.

The President shall designate a time and place for the meeting of such board, and shall cause due notice thereof to be given to the complainants and to the accused, and to all members of the district society of which the accused is a member.

A board of trial may hear fellows who appear in the interest of the accused, but legal counsel shall be excluded.

Failure of the accused to appear or be represented at the trial shall be considered *prima-facie* evidence of the truth of the charges, and a verdict may be rendered accordingly. In case of conviction, a board shall recommend such sentence as it shall deem best, as provided in Chapter I, Section 10. The Secretary shall enter on the records the proceedings of each board of trial, and shall report them to the Society at the next annual meeting for final action.

The Secretary shall notify the accused of the findings of a board of trial and of the action of the Society thereon; and he shall notify the several district societies of the sentence imposed.

Section 2. Each commissioner, and each prosecuting officer, shall be paid ten dollars a day for attendance, plus his incidental expenses.

It shall be a duty of any fellow summoned by the Committee on Ethics and Discipline to appear as a witness before a board of trial. No fellow shall be relieved of this duty without an excuse satisfactory to such a board.

CHAPTER IX

Amendments

These by-laws may be amended by a majority vote at any annual meeting of the Society, provided the proposed amendment or amendments shall have been submitted previously in writing to the Council, shall have been approved by that body by vote, and shall have been published and forwarded to each fellow, along with the program of the meeting of the Society whereat they are to be considered.

DEATH

BONNEY — Robert Bonney, M.D., of East Boston, died March 22. He was in his eighty-fourth year.

A native of Philadelphia, Dr. Bonney received his degree from Harvard Medical School in 1898. He was a fellow of the Massachusetts Medical Society and the American Medical Association.

He is survived by a brother.

WAR ACTIVITIES

CIVILIAN DEFENSE

First Aid for Air-raid Casualties

First-aid measures applicable to the emergencies of war are embodied in a booklet, *Handbook of First Aid*, issued by the Medical Division of the Office of Civilian Defense in co-operation with the American National Red Cross, for the use of enrolled civilian-defense workers.

The handbook is of pocket size and has twelve chapters titled as follows: "Advice to the Civilian Defense First Aid Workers"; "General Considerations"; "Care of Wounds"; "Dressings and Bandages"; "Hemorrhage"; "Burns"; "Shock (Collapse)"; "Fractures"; "Artificial Respiration"; "Transportation of the Injured"; "Chemical Warfare"; "Miscellaneous Conditions." As indicated by the titles, all material not relevant to the war emergency has been omitted from consideration. The book does not replace the standard Red Cross *Textbook of First Aid*, which is to be used in first-aid classes.

First-aid measures are described within the framework of the plan for emergency medical service: that is, they are described as they will be carried out under war conditions. Numerous illustrations clarify such procedures as the tying of bandages, pressure to stop hemorrhage, the application of traction splints and methods of transporting the injured. Throughout the handbook, the first-aid worker is cautioned against any action that should be left to a physician or any that would handicap the physician when he arrives. One of the cardinal principles emphasized is, Remember you are a first-aid worker and not a physician. For example, the worker is taught not to apply any antiseptic to a wound and not to apply an ointment or a salve to a burn.

About twenty pages are devoted to a discussion of fractures, with detailed descriptions of fixed traction splints for the upper and lower extremities, as well as improvised splints.

The chapter on chemical warfare describes types of war gases and lists briefly under each type the characteristic effects it produces and the appropriate first-aid measures. This chapter also includes instruction on care of burns caused by incendiary bombs containing phosphorus.

The last chapter covers heat stroke, heat exhaustion, heat cramps, frostbite and carbon monoxide poisoning. In connection with the injuries from heat and cold, it is pointed out that an enemy attack can occur at any season and that both victims and defense workers may be exposed to extremes of temperature for many hours.

CORRESPONDENCE

POLITICS: A PARALLEL TO MEDICINE

To the Editor: When we say that a man is a "good politician" we know what the term implies: that he is intellectually dishonest; that he is more or less a demagogue who plays on the passions of the people; and that he is untrustworthy, promising benefits that he knows are impossible to grant.

We have come to accept this standard set by the politicians as a necessary evil, as something unchangeable and permanent. We do not tolerate it in any other human relation or any other walk of life. Even the business and financial worlds, which are supposed to have low ethical standards, have a code of morals. A Wall Street broker is ostracized if he breaks his promise or his word in a financial transaction. A research worker in medicine who, to gain a temporary notoriety, intentionally publishes claims known by him to be false is forever outlawed by the profession.

For half a century, we have turned the country over to third-rate and fourth-rate politicians to govern. With a few exceptions, they have chosen politics as a career for reasons other than service to humanity. It is only necessary for a Lincoln to arise to be aware of the gulf between a man of integrity and vision — a man who not only would not lie but could not lie — and the army of men in the municipal, state and federal governments whose regard for telling the truth is mostly theoretical and whose conception of a promise is that it is a temporary expedient and can always be broken after a reasonable length of time. It is strange that politicians do not realize that there is no quality in a man either in public or private life that commands more intense respect and admiration than intellectual honesty. After many years in political life, a politician has compromised his principles so many times that he has ceased to have any principles. Ideals that he once may have had he is apt to view with derision and contempt. He becomes calloused and hard, and speaks the language of the street and gutter.

In the recent mayoralty election in New York City, a prominent politician, in a fifteen-minute radio address, called Mr. LaGuardia a demagogue, a mountebank, a hypocrite, a guttersnipe and a "mucker run amuck." Such freedom of expression seems to be peculiar not only to the vulgar and the low but to politicians as well.

To such men as these, — opportunists, demagogues, grafters and men whose word cannot be trusted, — humanity has entrusted its life, its freedom and its property. By their fruits they are known. The universal woe is a measure of their leadership.

And now a river of blood encircles the earth. And now our young men clean and strong and unbesmirched go forth to die in foreign lands by hideous ways to serve the ends of men called great. These, our sons, so innocent, so gay, shall water the earth with their blood. Guiltless, they are chosen to pay for our folly and greed. They shall lie stabbed and torn and shriveled with fire. Junes will come and go. They will not feel the hot sun or the south wind's warm caress. They will not see the meadows spotted with yellow and gold or the bobolink swaying on slender reed, or breathe the scent of pine and the new cut hay. They are the dead; and all the promise of their youth is blasted in the bud.

So this ignoble breed has set the style for politics in this country. We accept it as a matter of course. It never occurs to us that the style could be changed like women's hats. We have no vision and no conception of the change that would occur if a few thousand high-minded, cultured young people entered political life. If one has ever planted grass seed, one knows that if enough seed is planted only a few weeds will grow. If it is cultivated carefully, weeds will cease growing entirely.

Until recently, the educated and well-to-do classes of society in this country have had nothing to do with politics. It is a dirty business, and the better elements do not want to soil their hands with it.

A while ago, I read a history of medicine, and I noted a parallel between medicine as practiced one or two hundred years ago and politics, domestic and world politics, as practiced today. If we look on war as a plague and poverty and inequality of opportunity as a disease, we shall appreciate the similarity of the problem and the similarity of the attitude of the public toward it.

A hundred and fifty years ago, the average span of life was twenty years. It is now sixty. The principles of mod-

ern medicine were unknown. There was no sanitation. Pestilence and disease were present all the time. Every ten years or so, Europe was swept with one plague or another: bubonic plague, smallpox, typhus, typhoid fever and cholera came in their turn. Tuberculosis, diphtheria and scarlet fever in virulent form were endemic all the time. It is stated that one epidemic of bubonic plague in the Middle Ages removed a third of the population of Europe. In this country, at the beginning of the nineteenth century, an epidemic of yellow fever killed fifty thousand people in Philadelphia.

These plagues were thought to be due to acts of God, to punish the people for their sins. Cotton Mather was a strong exponent of this idea. Religion dominated medicine, and it was considered a blasphemy if anyone questioned an act of God, and made an effort to discover the cause of disease. To dissect a human body for the purpose of learning its anatomy was considered a desecration of the temple of God and was prohibited by law. So there was no chance of learning even the fundamentals of medical science.

People accepted plague, just as we today accept wars, as something inevitable. We hear that man is a fighting animal, and if the impulse to fight is curbed he will degenerate. The Nazis have said that war is a desirable thing, and hence they make a virtue of it.

In those days, doctors were, for the most part, ignorant men. The surgeon was a barber, and the physicians came from equally humble walks of life. Molière, in his plays, gives expression to the contempt of the public for the medical profession. The doctor was a constant butt for ridicule. The ridicule was justified, for he was more or less a humbug, just as the politician is today. He tried to cover up his ignorance by pomposity and putting on a front. He cultivated a bedside manner, used long words, and wrote his prescriptions in Latin. To impress his patients, he wore a high hat and frock coat and carried a gold-headed cane. He talked a jargon that would be entirely unintelligible to physicians today. His theories concerning the causes of disease and its treatment were almost entirely wrong. Very little of value has come down to us. For almost every ailment, he prescribed bleeding. A sick person in those days was indeed fortunate if he escaped the clutches of a physician.

A century ago, the causes of diseases were unknown. Every doctor had his private theory. It was usually in conflict with that of his confreres and gave rise to bitter controversies and ill-feeling in the profession. Today, we see the parallel of this among economists, politicians and "planners" of one kind or another. There are as many theories of economy today as there were theories of disease in the dark ages of medicine.

Up to a century ago, then, man was still living in the Middle Ages, so far as knowledge of the laws that govern disease and health is concerned. He knew no more about the causes of disease than had been known two thousand years before.

Then a miracle occurred. In France, out of the darkness a light shone out. Louis Pasteur had begun his work. For fifty years, he carried on his researches to determine the causes of disease in human beings and animals, the blight of the silkworm and the fermentation of wine. He opened up new worlds for science to explore and became the founder of modern medicine. At the beginning, he aroused tremendous opposition in the medical profession. His every contention was disputed. He was labeled a charlatan and a humbug. Surmounting the greatest abuse ever directed against any scientist, his ideas at last prevailed. A little group in England headed by Lister adopted his principles. Semmelweis in Austria put them into practice. Oliver Wendell Holmes in the United States listened and introduced his ideas to Boston.

One by one, the plagues that had decimated mankind for hundreds of years were brought under control. Out of the confusion and ignorance that medicine was a hundred years ago, — when superstition, quackery and the blind following of tradition were the chief characteristics of the profession, — has grown a mighty system of healing that has spread to all the corners of the earth. Medical science has no secrets; no discovery is patented. It has dedicated itself to the service of mankind. It advances by leaps and bounds. Every week, there is a new discovery. It may not be too rash to prophesy that the dream of the ages will be realized: that sickness and disease will be banished from the earth. Pasteur's precept still holds in laboratories, hospitals and medical schools the world over. It is very simple — on the hearts and minds of every research worker and medical student is written the command: "Seek the truth, follow the truth, tell the truth."

Might not the politicians, might not we all, learn something from the study of the history of medicine? In it, a century ago, one of the greatest revolutions in all history occurred. It was not like an ordinary upheaval, conditions reverting to their former state after a period of time. It was a permanent and beneficent revolution, which started an evolutionary process that with ever-widening circles has continued to this day. It set new standards; it created a new atmosphere in which reason, truth and knowledge flourished and flowered. It was democratic; it was international — medical men the world over speak the same language; it sought not to enrich itself; it was governed by no commercial motives; it built no monopoly; it sought only to create a better and healthier world for men and women to live in.

It is said that wars are inevitable and impossible to eradicate. Must not a mother have said two hundred years ago, sitting by the bed of her dying child, "It is an act of God; we must suffer for our sins"?

Following the work of Pasteur, thousands of young men of the highest type in all parts of the world began crowding into medical schools and laboratories as volunteers in the new crusade. Today, are our imaginations so feeble that we are unable to visualize the results of thousands and tens of thousands of honorable and intelligent young men and women entering political life, crushing by weight of numbers the forces of greed, dishonesty and hate that now rule the world? If grass seed is sown thickly enough, the weeds will not grow. When that happens, it will be the greatest of all crusades.

NEIL C. STEVENS, M.D.

Walpole, New Hampshire

REPORT OF MEETING

JEWISH MEMORIAL HOSPITAL

At a regular meeting of the Jewish Memorial Hospital in Roxbury on December 3, Dr. Joseph H. Pratt, of the Pratt Diagnostic Hospital, discussed "Recent Phases of Pancreatic Disease." He stated that the incidence of carcinoma of the pancreas is not nearly so rare as its clinical recognition indicates. It has been reported that 0.5 to 1.0 per cent of all autopsies reveal this condition. Engleman, in San Francisco, however, reported an incidence of 2.1 per cent of all post-mortem examinations and 9 per cent of all cancers found in the series. Its anatomic position

and relations make this organ difficult to palpate even in cases of cancer, but often result in signs and symptoms referable to the biliary tract or duodenum.

From a physiologic standpoint, Dr. Pratt said that the pancreas is an important factor in the digestive functions of the body. Its trypsinogen is converted by the enterokinase of the intestinal tract into the active enzyme, trypsin, which aids in the digestion of protein. In addition, there are diastase for the digestion of starches and lipase for that of fats. Furthermore, a useful alkaline medium, whose presence, incidentally, is often a more significant diagnostic point than that of the ferments, is supplied. The amount of fluid secreted may equal as much as 1500 to 2000 cc. per day, whereas the injection of secretin may call forth as much as 100 to 500 cc. in a single hour. The external pancreatic juices were formerly not considered essential for the maintenance of health and life, and are still ignored in most operations for carcinoma of the pancreas; this belief is now known to be a fallacy. Ligation of the pancreatic ducts results in an elevated blood diastase for several months, and huge doses of pancreatin (5 to 10 gm. daily) are necessary to offset this lack.

The elevation of the blood or urinary diastase has become a valuable test in the diagnosis of acute pancreatitis. This was first noted in 1922, when acute edema without necrosis was originally recognized, but is also present in acute hemorrhagic pancreatitis with fat necrosis. Failures in the use of this test can be attributed to the late application of the test or the late examination of the urine. Even if the disease is progressive, the diastase values return to normal after forty-eight hours at the latest, but they are invariably positive during the first twenty-four hours. The urine is more frequently positive than the blood, but must be examined within two hours of voiding. The importance of making the diagnosis is reflected in the statistics, which reveal a decrease in mortality from 60 or 70 to 25 per cent or less by refraining from operation in acute pancreatitis. The diastase values have been found significantly elevated in no other condition. The test should be carried out daily so that a curve rather than a single determination may be available for the following of a suspected case.

The stools serve as an excellent guide in cases of pancreatic disease and in differentiating jaundice from other causes. In any obstruction of the pancreatic juices, the stools are bulky, light colored and foul smelling. The lack of color persists even in the presence of sufficient bile from the biliary tract. Microscopically, there are fat globules and crystals, as well as muscle fibers, if meat has been ingested. This latter observation is essential in the differential diagnosis of tropical sprue, which is a disturbance in fat digestion only.

In acute edema of the pancreas, the epigastric pain is usually severe, but not agonizing, and can be controlled with morphine in contradistinction to acute hemorrhagic necrosis. The pain may easily be confused with that of acute gall-bladder colic and may be differentiated only by the diastase test. Again, the value of daily determinations is brought out, for if the values return to normal on the second or third day the diagnosis becomes clearer. Such attacks, however, are usually associated with cholecystitis, and the subsequent removal of an affected gall bladder should be carried out, to guard against recurrences and possible acute hemorrhage.

Dr. Pratt described the double-barreled gastroduodenal tube, which has proved so helpful in the study of the pancreatic secretions. It has openings in the stomach portion to allow for decompression of that organ, then a closed part, then openings in the duodenum that are drained through a separate tube and thus allow separate analysis of stomach and duodenal contents. In the normal person, the intravenous injection of secretin causes a rapid increase of the duodenal contents and a decrease in the amount of bile. Pure pancreatic juice is obtained only in the presence of a normal gall bladder. Normally, there is also a rapid rise in the duodenal alkalinity on the injection of secretin. This test has been employed in an attempt to diagnose carcinoma of the pancreas, in which all the functions of the gland are diminished. In 3 cases in which the stools did not indicate this disease, the secretin test revealed a low volume and a low alkalinity. Acute pancreatitis seems to run normal values in the limited number of cases observed. In cancer, the values for trypsin, lipase and diastase in the duodenal drainage are also low.

In discussing the diagnosis of carcinoma of the pancreas, Dr. Pratt pointed out that painless jaundice is greatly overstressed. Pain is actually a prominent symptom in approximately 60 per cent of cases, and may occur without jaundice. The diagnosis is seldom made without jaundice. In Engleman's series, loss of weight occurred in virtually 100 per cent of the cases, and this has been corroborated at the Pratt Diagnostic Hospital. The amount varies from 10 to 40 pounds. The second most constant finding in both series was that of abdominal pain. This is not characteristic in type, may occur anywhere in the abdomen, and is not necessarily constant. Jaundice is also found in about 60 per cent of cases but is present as a late sign, as shown by the fact that it was of less than six weeks' duration prior to death in over 65 per cent of Engleman's cases. Blood in the stools was found in 75 per cent of those at the Pratt Diagnostic Hospital but in only 13 per cent by Engleman. Dr. Pratt has also observed an elevated blood-sedimentation rate in 75 per cent of his cases, and diabetes in 25 per cent. Also noted was a tendency for the patient to be unduly nervous.

In answer to questions, Dr. Pratt stated that he believes that the sphincter of Oddi is really a sphincter and that the finding of pancreatic ferments in the gall bladder indicates an elevation of pressure. Probably a common channel is the explanation of the association of acute edema of the pancreas with biliary disease. He considers "acute hemorrhagic pancreatitis" a misnomer, the condition being one of intoxication rather than of infection. If such a patient is operated on inadvertently and the condition is recognized,— which should always be easy,— the abdomen should be closed immediately, without exploration or drainage.

BOOK REVIEW

The Microbe's Challenge. By Frederick Eberson, Ph.D., M.D. 4°, cloth, 354 pp., with 1 portrait. Lancaster, Pennsylvania: The Jaques Cattell Press, 1941. $3.50.

Of all the popular books on bacteriology written in recent years, the reviewer considers this publication outstanding. Soundly and accurately written, in language only technical enough to make the meaning clear, the work covers the entire field of microbes and their relation to illness in man. A glossary, index and suggested readings complete the volume. There are no illustrations, a fact that does not detract from the value of the book. Here is a publication that will appeal to any intelligent layman and should find a place in every public library as a standard reference text.

(Notices on page x)